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VOLUME 24 NUMBER 2

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Archives of Internal Medicine

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IMMUNITY OF CITY-BRED RECRUITS*

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AND

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I. THE DATA

I. CONDITIONS UNDER WHICH DATA WERE OBTAINED

The presence in our country, during the last four months of 1917, of bodies of men mobilized in army camps gave an opportunity to observe the development of epidemics in crowded communities. The conditions afforded for such study were unusual in all respects, and will probably not be met again for a long time. In the first place, the population of the respective camps came, for the most part, from definitely known areas; so that something could be said about the nature of the population, whether prevailingly rural or urban, and whether from southern states or northern. Indeed, for the most part it could be stated what state or group of states was tributary to a particular camp. In the second place, the entire population was daily inspected and every inducement offered for those suffering from any ailment to go on sick report. Moreover, all cases of admission to sick report were recorded by medical officers and the records sent to the office of the Surgeon-General in Washington, where all records were assorted and treated statistically. A preliminary account of the results gained from the analysis of such reports was printed in a report of the Surgeon-General of 1917. The statistics of 1918 will appear toward the end of the present year in the annual report of the Surgeon-General. However, it appears worth while to lay emphasis on and to develop somewhat more extensively certain conclusions that flow from an examination of the medical statistics of the military camps and cantonments for 1917.

The population of the camps was fairly homogeneous, consisting of men aged from 21 to 30 years, taken direct from civil life, and placed either in barracks (where they slept in beds that were only about six feet apart), or in tents where they were often given an

* Prepared in the Section of Medical Records, Medical Department, U. S. Army, and published by permission of the Surgeon-General.

average of less than 50 square feet of space. For men who came from cities, with their crowded factories, offices and shops, this necessary economy of space per man was not novel; but many men from rural districts had never before lived and moved in the midst of such large masses of men. At any rate, the difference in reaction to disease of men from rural and urban districts was striking.

In this paper it is proposed to consider the relative incidence of measles, mumps, lobar pneumonia, cerebrospinal meningitis and scarlet fever and also brief reference will be made to influenza in the camps during the fall of 1917 and the winter of 1917-18. Next will be considered the incidence of these diseases, taken together, in various camps. And, finally, the probable cause of the diversity in incidence of these various diseases in the different camps will be treated. We shall take up, first, then, the six principal epidemic diseases.

II. DETAILS OF DATA FOR SIX COMMUNICABLE DISEASES

(a) Measles.—Measles has always been a great camp scourge, and it was, therefore, in accordance with expectation that a great epidemic of measles affected our army camps in the winter of 1917-18. This epidemic began for some of the camps in October, for others in December, and persisted to January for some and to February and March for others. Before the first of January there had been more than 47,000 cases of measles among the enlisted men in the United States. As stated, the incidence of measles varied greatly in the different camps. This ranged in 1917 all the way from a mean annual admission rate of 500 per 1,000 at Camp Wheeler, Ga., to about one at Camp Wadsworth, S. C. The climatic and housing conditions at these two National Guard camps, located about only 100 miles apart, were very similar. Measles was present at both camps. The tremendous difference in the history of the epidemic seems clearly to be due to a difference in the constitution of the population. The soldiers at Camp Wadsworth were seasoned National Guard troops from New York City and vicinity. The soldiers at Camp Wheeler were mainly newly inducted National Guard troops from Alabama, Florida and part of Virginia, sparsely settled states.

The returns of admission to sick report give the nativity of the patients. It is therefore possible to indicate on a map the number of patients having measles in any camp that were born in each of the states. However, this figure would not have great significance in view of the great variation in the number of native-born sons contributed by the various states. We may supply the deficiency roughly by making the assumption that the number of men in the army born in any state is proportional to the present number of males, age from 20 to 30, in the present population of the state. This assumption has

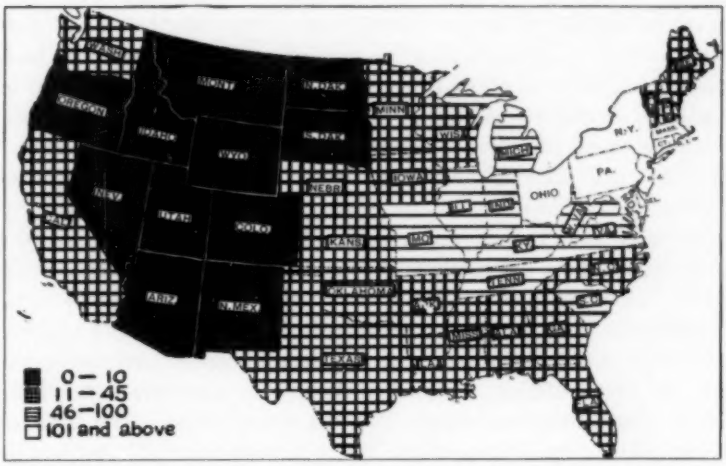

Fig. 1.—Map of the United States indicating relative density of the different states in four grades. The legend indicates the number of inhabitants per square mile. The lighter areas represent the regions of greater density of population; the darker areas, of least density.

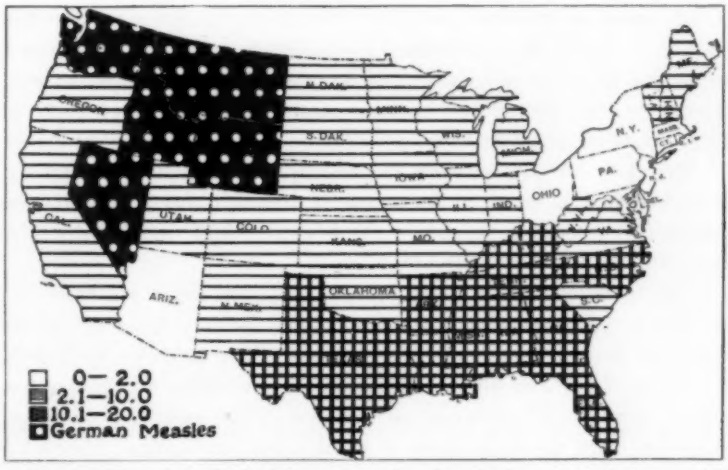

Fig. 2.—Map of the United States showing distribution of admission to sick report for measles by states of nativity of enlisted men, rate per 100,000 of the adult male civil population of each state, age from 20 to 29 years, census of 1910. In three grades. The darker areas represent greater incidence of the disease.

certain large errors, particularly in those western states that have developed rapidly in the past twenty years; but, owing to the fact that there is internal evidence that the state of origin has sometimes been recorded in place of native state, it seems, perhaps, over refinement to make the correction. A map of distribution of measles by native state has been drawn following the suggested method (Fig. 2). In Figure 1 is given a map showing the distribution of the population of the United States by states in four different grades. The comparison of the map of measles with map of density of population shows points of close similarity. Thus, the southern New England States and the Middle States, including Maryland and the State of Ohio, are those of dense population. They are also states with the lowest incidence of measles. The southern Atlantic and Gulf States are those of relatively low density of population. South Carolina has, however, a relatively denser population than North Carolina and Georgia. The table of distribution of measles shows the South Atlantic and Gulf States to be states of high incidence of measles in camps, but South Carolina has relatively less measles than North Carolina and Georgia. There was relatively little true measles in the last three months of 1917 at Camp Lewis, despite the fact that it draws men from a sparsely settled territory. In place of true measles there was a striking epidemic of German measles at Camp Lewis, and the nativity of sufferers from this disease at that camp is indicated by the black area in the northwest section of the map of measles. It may be added that after the subsidence of the epidemic of German measles there occurred early in 1918 a medium sized epidemic of ordinary measles at Camp Lewis.

The close relation between the density of the population and the immunity from measles is the strongest argument for attributing the immunity of measles in camps to the antecedent immunization by exposure to measles in early life.

That persons coming from densely populated areas are more apt to have had measles than those from rural districts is shown by the census of mortality statistics. According to these statistics, in densely populated states like Rhode Island and Connecticut, deaths (and it may be properly inferred cases of sickness) from measles occur at an early age. On the other hand, in rural states like Kansas, Kentucky, Maine and Virginia, deaths occur relatively later in life. This relation between the ages of deaths from measles in urban and rural states is well brought out in Table 1.

TABLE 1.—COMPARATIVE DISTRIBUTIONS OF DEATHS FROM MEASLES BY AGE GROUPS IN URBAN AND RURAL STATES, "MORTALITY STATISTICS," 1915

	Total Deaths, Measles	Under 1 Year	1 Year	2 Years	3 Years	4 Years	5 to 9 Years	10 to 19 Years	20 to 29 Years	30 to 39 Years	40 to 49 Years	50 to 59 Years	60 to 69 Years	70 to 79 Years	Per Cent. of Deaths Over 10 Years
Urban States															
Rhode Island...	60	19	21	12	3	1	3	.....	.....	.....	.....	.....	.....	.....	0.0
Connecticut.....	61	16	26	7	3	2	3	2	1	1	.....	.....	.....	.....	6.7
Rural States															
Kansas.....	73	17	12	10	5	8	6	4	2	2	2	2	1	1	20.6
Kentucky.....	85	18	19	11	2	5	5	9	6	2	1	5	2	.....	29.4
Maine.....	18	2	7	2	1	1	3	.....	.....	.....	1	.....	.....	1	11.1
Virginia.....	58	10	6	13	2	3	5	11	4	1	.....	2	1	.....	32.7

Again, if the states of the registration area of the United States be arranged in rank in respect to the amount of urban population (Table 2), it appears that the proportion of all deaths that are due to measles diminishes on the whole as the percentage of urban population does, while the average age at death from measles increases on the whole inversely with the percentage of rural population. Of course,

TABLE 2.—MEASLES, CIVIL LIFE, PROPORTION OF EACH STATE THAT IS URBAN OR RURAL IN RELATION TO INCIDENCE OF DEATHS FROM MEASLES AND AVERAGE AGE AT DEATH FROM MEASLES, MORTALITY STATISTICS, 1915. U. S. CENSUS

Rank of States in Urban Population	Percentage Urban	Measles per Cent. of All Deaths	Average Age at Death from Measles
1. Rhode Island	812	0.673	2.53
2. Massachusetts	782	0.511	3.15
3. New York	763	0.604	3.04
4. New Jersey	650	0.565	2.44
5. Connecticut	608	0.334	3.20
6. California	429	0.398	6.42
7. Ohio	485	0.331	4.94
8. Pennsylvania	480	0.491	2.45
9. Maryland	477	0.150	4.12
10. Michigan	398	0.257	3.85
11. Colorado	624	0.198	3.71
12. Missouri	370	0.378	7.79
13. Wisconsin	343	0.199	4.48
14. Minnesota	334	0.382	5.61
15. Indiana	330	0.195	6.68
16. Maine	231	0.150	9.20
17. Virginia	208	0.189	9.95
18. Kansas	196	0.401	9.02
19. Kentucky	181	0.341	11.00

there are fluctuations on the series, as for example, California; but this is a state of great cities and also great farming areas. So, also, Missouri, while prevailingly rural, is elevated to an unduly high place in the scale of urbanity owing to the two great cities that lie on its borders; consequently, it has an unduly high average of death from measles, though a fairly high proportion of the deaths of the state are due to measles.

Again, the relation between density of population and immunity from measles may be shown by applying the mathematical theory of chance and by calculating the correlation between the proportion of men in the army born in any state who were admitted to sick report for measles, on the one hand, and the urbanity of their respective native states on the other hand. The correlation between these two conditions was calculated from Table 2, and the figure of correlation found to be —80 per cent., a high correlation as correlations go, but inverse (as the minus sign signifies), meaning that the more urban the native state the less susceptible to measles its native born sons in the army (Table 3).

TABLE 3.—Correlation Between Admission Rate by State of Nativity and Percentage of Urbanity of the State

Per Cent. of Urbanity of State	Measles: Total Admission Rate by State of Nativity					Deviation	Frequency
	0 to 4.9	5 to 9.9	10 to 14.9	15 to 19.9	20 to 24.9		
10 to 19.9	1	4	1	3	2	—30	11
20 to 29.9	1	2	3	1	2	—20	10
30 to 39.9	1	2	..	..	1	—10	4
40 to 49.9	1	6	2	..	..	0	9
50 to 59.9	2	4	..	..	..	10	6
60 to 69.9	1	2	..	..	..	20	3
70 to 79.9	2	..	..	..	..	30	2
80 to 89.9	1	..	..	..	..	40	1
90 to 99.9	3	..	..	..	..	50	3
Frequency.....	13	21	6	4	5	..	49

(b) Mumps.—Mumps is one of the commonest infectious diseases in army camps. During 1917 it made up 4.4 per cent. of the total admissions to sick report in the United States, and 11.0 per cent. in Europe.

TABLE 4.—Admissions, National Guard and National Army, Selected Camps

	September	October	November	December
National Guard—				
Camp Beauregard.....	2	32	466	1,299
Camp Wheeler.....	6	17	301	1,923
Camp Bowie.....	14	111	542	1,035
Camp Shelby.....	1	66	331	383
National Army—				
Camp Lee.....	1	7	276	990
Camp Travis.....	3	45	338	943
Comp Jackson.....	24	53	82	358
Comp Pike.....	4	1	123	344

In the camps mumps was present in slight degree in September. The number of cases had more than doubled in October, more than quadrupled in November over the preceding month, and increased in nearly the same ratio in the following month (Table 4). The maximum cases of admissions increased in many of the camps in January, 1918. After this there was a decline in number of new admissions.

The relative incidence of mumps at camp among the natives of the different states is indicated in Figure 3. It will be found instructive to compare this with Figure 1, showing the distribution of density of population. It appears at once that the densely populated states of southern New England and the Middle States are just those whose sons were most immune to mumps. On the other hand, the Southern Atlantic and Gulf States show a high incidence of mumps in states of sparse population. Louisiana and North Carolina have, for some

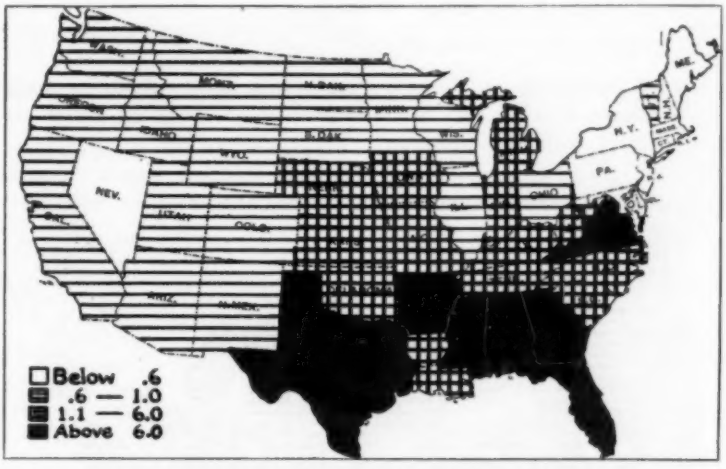

Fig. 3.—Map of the United States showing distribution of admission to sick report for mumps at National Army Camps, 1917, by state of nativity of enlisted men, rate per 100,000 of the adult male civil population of each state, aged 20 to 29 years, charted in four grades. The darker areas indicate greater incidence of the disease.

unexplained reason, a lower incidence for mumps than the sparseness of their population would warrant us in predicting. The relation between density of population and immunity breaks down if an attempt is made to apply it to the sparsely settled western areas, a result which may be in part due to the recent immigration into these states, which makes the divisor used (of current population instead of actual number born) too large, and hence the quotient too small.

The correlation between urbanity and admission for mumps is shown in Table 5. From this table the correlation was found to be —58, which again is a rather large correlation.

TABLE 5.—Correlation Between Admissions for Mumps by State of Nativity and Percentage of Urbanity of the State

Per Cent of Urbanity of States*	0 to 2.9	3 to 5.9	6 to 8.9	9 to 11.9	12 to 14.9	Deviation	Frequency
10 to 19.9	2	4	2	1	2	—30	11
20 to 29.9	..	5	3	..	2	—20	10
30 to 39.9	2	2	..	..	..	—10	4
40 to 49.9	5	4	..	..	..	0	9
50 to 59.9	5	1	..	..	..	..	6
60 to 69.9	3	..	..	..	..	..	3
70 to 79.9	2	..	..	..	..	..	2
80 to 89.9	1	..	..	..	..	..	1
90 to 99.9	3	..	..	..	..	..	3
Frequency.....	23	16	5	1	4	..	49

* See Table 6 for names of states.

(c) Lobar Pneumonia.—Lobar pneumonia occurs either as a primary disease or secondary to measles and other epidemic diseases. It is, indeed, a tenable hypothesis that the symptoms of lobar pneumonia in young men of military age usually appear only after some event that has diminished resistance, such as disease of the respiratory

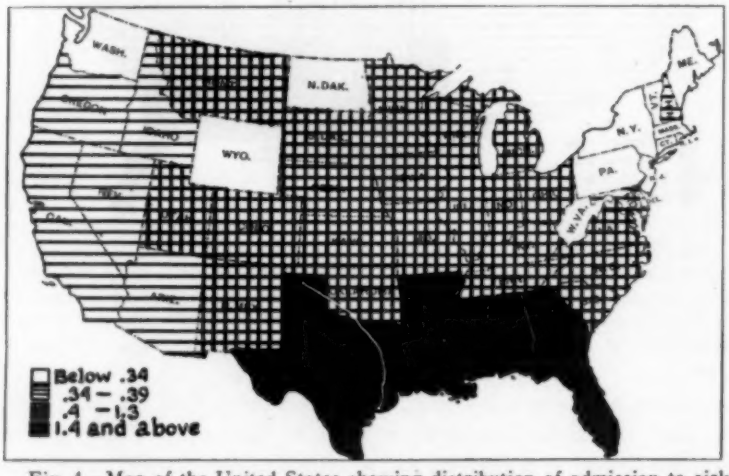

Fig. 4.—Map of the United States showing distribution of admission to sick report for lobar pneumonia (primary) in National Army camps, 1917, by state of nativity of enlisted men, rate per 100,000 of the adult male civil population of each state, aged 20 to 29 years, census of 1910, charted in five grades. The darker areas indicate the greater incidence of lobar pneumonia.

tract, overwork, or exposure. In the present section we shall consider, however, those cases of primary lobar pneumonia, that is, those for which no antecedent disease was reported.

The incidence of lobar pneumonia in the different camps varies greatly, as in the case of measles and mumps; camps which, like Bowie

(Texas), Wheeler (Georgia), Pike (Arkansas), Travis (Texas) drew from a rural territory had much lobar pneumonia, while camps which, like Devens, Wadsworth, Dix and Upton, drew from densely populated areas, had relatively few cases of lobar pneumonia.

These relations are brought out graphically in Figure 4, which shows the distribution of the different degrees of incidence of lobar pneumonia according to the nativity of the patients. One sees again that the densely populated area of Southern New England and Middle States have few cases of lobar pneumonia, while the Gulf States show high incidence. The very sparsely settled states of the Great Basin have an intermediate amount of lobar pneumonia among their recruits.

TABLE 6.—CORRELATION BETWEEN RATE OF ADMISSION FOR LOBAR PNEUMONIA BY STATE OF NATIVITY AND PERCENTAGE OF URBANITY OF THE STATE (BASED ON TABLE 11, P. 476, S. G. REP., 1917)

State	Per Cent. of Urbanity	0 to 0.50	0.51 to 1.00	1.01 to 1.50	1.51 to 2.00	2.0 to 2.50	2.51 to 3.00	3.51 to 4.00	4.01 to 4.50	4.51 to 5.00	5.0 to 5.5	Deviation	Frequency
Miss., Ark., S. D., N. Mex., N. C., S. C., Nev., Ala., W. Va., Okla.	10 to 19.9	..	2	7	1	1	..	..	..	..	..	0	11
Tenn., Ga., Ida., Va., Tex., Ky., Neb., Fla., Kan., Wyo.	20 to 29.9	..	2	3	3	1	..	..	..	..	1	0	10
La., Iowa, Ariz., Mont.	30 to 39.9	..	..	2	2	..	..	..	..	..	..	0	4
Minn., Ind., Mo., Wis., Ore., Utah, Mich., Vt., Del.	40 to 49.9	1	5	3	..	..	..	..	..	..	..	0	9
Colo., Md., Me., Wash., Ohio, N. H.	50 to 59.9	..	3	3	..	..	..	..	..	..	..	0	6
Pa., Ill., Calif.	60 to 69.9	..	2	1	..	..	..	..	..	..	..	0	3
N. J., N. Y.	70 to 79.9	..	2	..	..	..	..	..	..	..	..	0	2
Conn.	80 to 89.9	..	1	..	..	..	..	..	..	..	..	0	1
Mass., R. I., D. C.	90 to 99.9	..	3	..	..	..	..	..	..	..	..	0	3
Frequency	.....	1	20	19	6	2	..	..	..	..	1	0	49

The correlation between incidence of lobar pneumonia and density of the states in which the patients were born is shown in Table 6. The calculation correlation coefficient from this table gives —0.37, a relatively high inverse correlation.

The reason for this relation between incidence of lobar pneumonia and density of states will be discussed later. In the present connection it is worth while to point out that there is no such marked differences in the age distribution of deaths from lobar pneumonia in civil life that has been shown in Table 1 in the case of measles. This is brought out in Table 7, which gives for three urban and four rural states the total number of deaths and the number of deaths occurring at successive years of life. The data have been taken from the morbidity statistics of the census of 1915. Besides the number of deaths occurring at each successive period of life, there is given the proportion that the deaths over ten years are to the total deaths in the state.

A comparison of the sums of the three urban states and the four rural states shows no obvious differences between them. It appears to be true that in urban states there is a slightly lower mortality from lobar pneumonia under thirty years and a slightly higher mortality over thirty years of age than in the case of rural states.

TABLE 7.—LOBAR PNEUMONIA: TOTAL NUMBER OF DEATHS AND TOTAL NUMBER OF DEATHS AT VARIOUS AGES IN THREE URBAN AND FOUR RURAL STATES

States	Total Deaths	Under 1 Year	1 Year	2 Years	3 Years	4 Years	5 to 9 Years	10 to 19 Years	20 to 29 Years	30 to 39 Years	40 to 49 Years	50 to 59 Years	60 to 69 Years	70 to 79 Years	80 to 89 Years	90 to 99 Years	100 Years and Over	Per Cent. of Deaths Over 10 Years
Mass.	3,224	310	160	50	31	16	45	70	175	279	372	421	556	482	211	27	1	
R. I.	374	30	15	3	7	5	8	9	23	34	45	72	63	47	11	2	0	81.82
Conn.	945	92	32	17	9	4	10	19	63	86	143	132	147	121	57	11	2	82.65
Urban	4,543	432	216	70	47	25	63	107	261	399	560	625	766	650	279	40	3	81.22
Kansas	620	75	26	9	4	6	7	27	40	54	39	76	99	112	41	4	1	79.52
Ky. (white)	770	83	33	19	10	5	19	45	42	58	62	80	126	129	55	4	0	77.75
Maine	411	32	11	6	2	6	9	19	22	35	44	44	74	64	36	7	0	83.74
Va.	419	27	9	5	6	3	11	22	39	27	49	52	73	69	26	1	0	85.41
Rural	2,220	217	79	39	22	20	46	115	143	174	194	252	372	374	158	16	1	80.59

(d) Cerebrospinal Meningitis.—This disease is more important on account of its high case mortality than on account of its frequency. In the army of 1917, 31 per cent. of those men diagnosed as having cerebrospinal meningitis died. The total number of admissions was 971. If the camps be compared in respect to the incidence of cerebrospinal meningitis it is found that camps drawing from densely populated areas, such as Camps Upton, Dix, Devens and Wadsworth, stand at the bottom of the list, while Jackson, South Carolina, Beauregard, Louisiana, stand at the head of the list.

The details of relative incidence of cerebrospinal meningitis by state of origin of the different troops is shown in Figure 5. This figure is drawn up in a different fashion from the preceding one. The basis of the map is the relative frequency of occurrence of cerebrospinal meningitis in the different camps, that is, the morbidity rate. This morbidity rate is assumed to be distributed uniformly over the states that are tributary to the camp. The territory tributary to each camp is shown in Figure 6. This method conceals individual differences between adjacent states, but it brings out differences that are due to variations in diagnosis and reporting at the different camps. Thus, it seems probable that Camp Gordon drawing from Tennessee, Georgia and part of Alabama, had a relatively small amount of cerebrospinal meningitis, possibly through greater attention to the isolation of

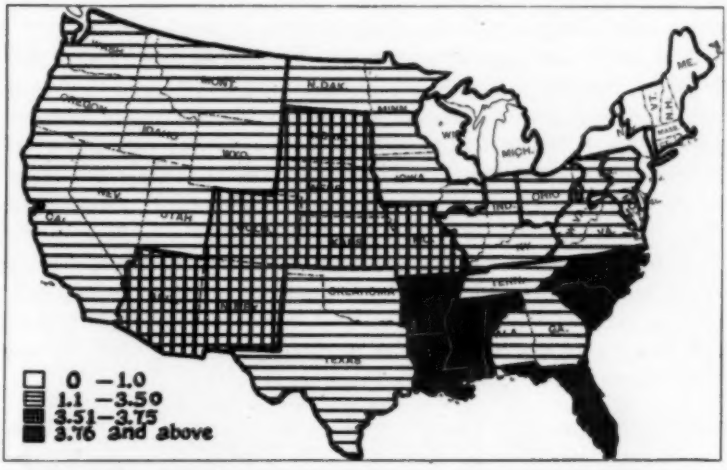

Fig. 5.—Map of the United States showing distribution of morbidity rate for cerebrospinal meningitis in National Army camps, 1917, by states from which the camps drew their troops, charted in four grades. The darker areas indicate greater incidence of the disease.

Fig. 6.—Map of the United States showing the territory tributary to each of the National Army camps, 1917.

incipient disease or carriers. Camp Pike, on the other hand, had a great deal of this disease which gained extensive headway in the camp after it had, probably, been imported from another camp.

If Figure 5 be compared with Figure 1, it will be seen at once that the areas of southern New England, New York and New Jersey show the greatest immunity to cerebrospinal meningitis, and are at the same time among the most densely populated areas. Michigan and Wisconsin, which are intermediate in population, had relatively few cases. On the other hand, the south Atlantic and Gulf States had, on the whole, a high incidence of cerebrospinal meningitis. The same is true of the western states, east and south of the Rocky Mountains. With certain irregularities and exceptional cases, therefore, it is generally true that recruits coming from the most thickly populated sections of the country were less susceptible to cerebrospinal meningitis than those coming from more sparsely settled areas.

TABLE 8.—Correlation Between Rate of Admissions for Cerebrospinal Meningitis, Total Admissions and Urbanity of State

Per Cent. of Urbanity of States	0 to 0.09	0.10 to 0.19	0.20 to 0.29	0.30 to 0.39	0.40 to 0.49	Deviation	Frequency
10 to 19.9	..	3	2	3	1	—30	9
20 to 29.9	1	2	2	1	2	—20	8
30 to 39.9	..	1	..	1	1	—10	3
40 to 49.9	2	2	1	..	1	0	6
50 to 59.9	..	1	2	..	..	10	3
60 to 69.9	..	3	..	..	..	4	3
70 to 79.9	2	..	..	..	..	..	2
80 to 89.9	..	..	1	..	..	..	1
90 to 99.9	1	..	..	..	..	..	1
Frequency.....	6	12	8	5	5	..	36

No cases from Alaska, Delaware, District of Columbia, Idaho, Maine, Vermont or Wyoming. Two cases or fewer from Montana, Nevada, New Hampshire, North Dakota, Rhode Island, Utah and Washington.

The correlation between admission for cerebrospinal meningitis and urbanity of the native state is shown in Table 8. The correlation has been calculated from this table and found to be —0.44, a somewhat smaller correlation than in the case of measles and mumps.

(a) Scarlet Fever.—There were no epidemics of scarlet fever among the army camps in 1917. The total number of admissions among troops in the United States was indeed only 1,966. The incidence of the disease differed a good deal in the different camps. Figure 7 shows the relative frequency of the disease among men coming from different parts of the country. Here, again, we note that men from New England and the more thickly settled parts of New York State had little scarlet fever, and the same is true of men at Camps Lee, Jackson, Gordan and Taylor. In the case of Camps Jackson and Gordon, at least, the areas drawn from were relatively sparsely settled. On the other hand, the states tributary to Camp

Pike give a high incidence of the disease, and the same is true of the states tributary to Camp Lewis, and both these territories are relatively sparsely settled. While it seems clear that pains taken at the camps to prevent the spread of scarlet fever is one important factor in determining its relative frequency in the different camps, still its infrequency among troops coming from the densely populated parts of the country suggests that such recruits had a relative immunity to scarlet fever. It may be added that since the colored race is relatively resistent to scarlet fever the small amount of scarlet fever among troops from the South Atlantic states is probably in part due to the considerable admixture of the colored race in recruits from those states.

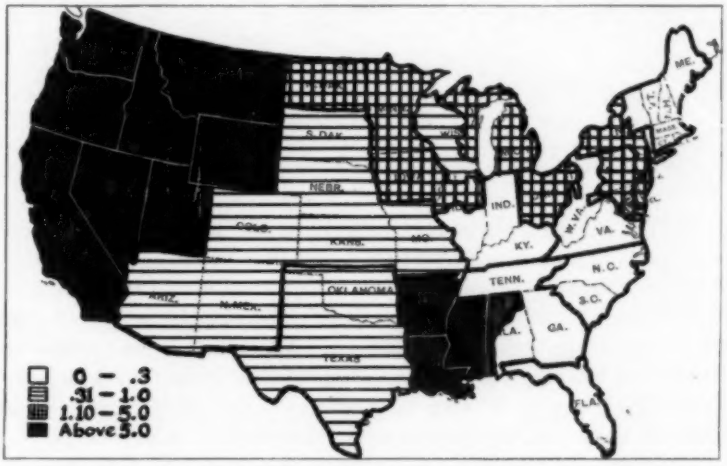

Fig. 7.—Map of the United States showing distribution of morbidity rate for scarlet fever in the National Army camps, 1917, by states from which each camp drew its troops, charted in four grades. The darker areas indicate the greater incidence of the disease.

(f) Influenza.—No detailed studies were made by the surgeon-general's office on the distribution by state of nativity of the cases of influenza that appeared in camp in 1917. A detailed study of the epidemic of influenza in 1918 is in course of preparation. Use may, however, be made of the imperfect and provisional telegraphic reports on influenza received by the surgeon-general's office during the autumn of 1918. An examination and tabulation of these reports indicates that even in the case of the pandemic influenza, camps that harbored chiefly recruits from rural states, in October and November, 1918, suffered worse than those that harbored mostly recruits from urban states. These facts are shown in Table 9.

TABLE 9.—Comparison of Five Camps Drawing Chiefly from Urban States and Five Camps Drawing Chiefly from Rural States, Giving Mortality and Morbidity in Relation to the Influenza Pandemic, Sept. 20 to Dec. 31, 1918. From Telegraphic Reports to the Surgeon-General's Office (Approximate Only)

	Diseases			
	Influenza Admissions	Pneumonia Admissions	Deaths (All)	Admission Rate (Aver.)
Urban Camps—				
Wadsworth	1,382	474	88	2,204
Devens	5,519	1,912	822	3,443
Dix	5,917	2,250	821	1,879
Meade	9,696	2,937	809	2,488
Upton	9,383	1,288	410	3,287
Total	31,897	8,901	2,950	13,301
Rural Camps—				
Beauregard	4,426	1,134	444	4,177
Dodge	9,550	1,622*	716	3,709
Funston	13,617	1,946	911	2,400
Grant	9,656	2,687	1,086	2,406
Travis	6,905	2,562	221	4,393
Total	44,154	9,952	3,380	17,085

* This included one missing report estimated as 500.

While too much stress may be paid on the precise results of the preliminary figures given in Table 9, still they suffice to indicate that the prevailingly rural camps (of which two were located in the South) had at least 25 per cent. more cases of influenza, 10 per cent. more pneumonia, 10 per cent. more deaths and 30 per cent. higher admission rate for all sickness than the prevailingly urban camps (of which one was in the South). It may be concluded, consequently, that in the influenza pandemic rural troops suffered more than urban troops.

III. TOTAL EPIDEMIC DISEASES IN CAMPS

As a sort of summary of the preceding sections and for the purpose of supplying certain additional data, Table 10 has been drawn up. This gives the ratios of incidence of the mentioned diseases for October, November and December, 1917, for the sixteen National Army camps. By referring to Figure 6, compared with Figure 1, it will be easy to see which camps drew from a prevailingly rural and which from a prevailingly urban territory. A glance will show that the large ratios are apt to occur in the camps that draw from the sparsely settled areas east of the Mississippi river. The general relation which we have considered between the sparsely settled areas and incidence of communicable diseases does not, it will be noted, hold in detail for the territory west of the Mississippi river. Thus, Camps Funston and Lewis were not noteworthy for a large disease rate. This is probably

TABLE 10.—Annual Rates Per 1,000 Men for Certain Camps by Special Diseases for October, November and December, 1917. (Absolute Numbers Are Given in Table 52, Surgeon-General's Reports, 1918)

Camp	Bronchopneumonia				Lobar Pneumonia				Measles, Uncomplicated				Measles Complicated with Bronchopneumonia			
	Oct.	Nov.	Dec.	Total	Oct.	Nov.	Dec.	Total	Oct.	Nov.	Dec.	Total	Oct.	Nov	Dec.	Total
Custer, Mich.	.....	.....	0.54	0.21	6.23	4.69	6.51	5.86	17.30	72.95	95.49	64.83	.....	.....	6.54	6.21
Devens, Mass.	0.45	3.58	3.13	2.39	3.59	3.13	4.02	3.56	0.90	14.75	73.79	29.84	.....	.....	.....	.....
Dix, N. J.	0.51	0.52	1.14	0.71	2.02	2.08	8.52	4.06	1.52	2.08	13.64	5.47	.....	.....	.....	.....
Dodge, Iowa	2.74	1.64	0.69	1.77	19.20	22.45	33.15	24.33	10.97	43.26	172.64	68.47	0.55	0.55	.....	0.39
Funston, Kan.	0.57	2.34	2.27	1.61	15.41	22.58	6.05	14.68	6.28	57.61	23.44	26.61	0.86	2.72	1.51	1.61
Gordon, Ga.	0.76	2.68	2.55	2.22	9.89	6.24	6.55	7.14	45.62	86.94	180.20	118.95	.....	0.45	7.65	3.49
Grant, Ill.	1.75	1.03	1.73	1.51	7.88	7.72	12.13	9.06	1.75	6.69	80.30	26.18	.....	.....	1.16	0.34
Jackson, S. C.	0.94	12.59	7.43	7.03	3.77	9.32	11.34	8.35	98.03	402.33	95.77	192.82	.....	13.52	2.74	5.27
Lee, Va.	.....	.....	5.31	1.78	0.46	7.26	16.38	8.14	0.46	87.99	96.50	62.88	.....	0.43	3.54	1.33
Lewis, Wash.	2.28	3.31	2.06	2.56	10.44	10.60	8.22	9.78	3.59	13.58	27.06	14.55	.....	.....	.....	.....
Meade, Md.	0.73	1.54	2.71	1.88	2.18	9.64	16.62	11.13	4.36	18.50	37.99	23.99	0.73	.....	0.34	0.29
Pike, Ark.	2.14	7.82	16.18	9.39	30.45	62.56	65.11	54.56	499.46	793.22	499.60	600.33	10.68	21.72	19.73	17.89
Sherman, Ohio	0.78	2.62	3.98	2.50	10.56	20.22	24.23	18.52	3.52	17.22	53.88	25.52	.....	.....	.....	.....
Taylor, Ky.	3.23	0.54	6.77	3.47	17.76	11.36	25.96	18.25	48.44	292.74	193.00	177.62	2.15	8.66	12.98	7.85
Travis, Texas	3.27	5.56	9.52	6.30	29.00	44.67	71.97	49.57	14.50	929.63	496.19	515.01	0.47	12.22	6.85	6.97
Upton, N. Y.	0.43	0.49	1.70	0.89	2.59	3.91	12.31	6.40	0.43	2.93	15.70	6.55	.....	0.49	1.27	0.60
Totals	1.29	3.04	4.44	2.97	10.87	16.32	20.84	16.15	47.94	185.72	136.27	122.87	0.88	3.87	3.72	2.87

Camp	Measles Complicated with Lobar Pneumonia				Measles with Complications Other than Pneumonia				Cerebrospinal Meningitis (Epidemic)				Mumps			
	Oct.	Nov.	Dec.	Total	Oct.	Nov.	Dec.	Total	Oct.	Nov.	Dec.	Total	Oct.	Nov.	Dec.	Total
Custer, Mich.	.....	.....	.....	.....	.....	2.01	2.17	1.46	2.08	.....	0.54	0.84	38.06	44.85	45.58	43.06
Devens, Mass.	.....	.....	0.45	0.15	.....	.....	.....	.....	.....	.....	1.34	0.45	0.45	2.68	5.27	2.83
Dix, N. J.	.....	.....	.....	.....	.....	.....	0.57	0.18	.....	.....	.....	.....	.....	3.11	5.11	2.65
Dodge, Iowa	.....	0.55	2.76	0.98	1.10	1.64	4.14	2.16	2.74	.....	8.29	3.34	4.39	31.76	82.87	36.49
Funston, Kan.	.....	0.39	0.76	0.34	0.29	2.34	0.38	0.92	4.57	8.17	0.38	4.38	9.99	8.17	3.40	7.46
Gordon, Ga.	.....	0.45	2.18	1.11	0.76	0.89	1.09	0.95	1.52	0.89	5.82	3.17	7.60	5.80	11.28	8.56
Grant, Ill.	.....	.....	.....	.....	.....	.....	.....	.....	0.44	2.57	0.58	1.17	29.32	4.63	10.98	15.94
Jackson, S. C.	1.41	3.73	.....	1.61	1.89	21.44	8.00	10.55	.....	9.32	41.44	18.46	24.98	38.23	139.95	72.24
Lee, Va.	.....	1.28	2.66	1.33	.....	2.14	1.77	1.33	1.39	0.85	1.77	1.33	3.24	117.90	438.25	188.34
Lewis, Wash.	.....	.....	0.34	0.11	0.33	0.33	1.03	0.56	0.98	2.98	4.45	2.78	4.90	12.92	28.09	15.11
Meade, Md.	.....	.....	.....	.....	.....	0.39	.....	0.14	.....	0.39	3.73	1.73	0.73	4.24	14.58	7.95
Pike, Ark.	8.55	13.47	16.97	13.42	4.81	15.64	11.44	11.03	2.14	6.52	5.13	4.77	0.53	58.43	135.75	69.77
Sherman, Ohio	.....	.....	.....	.....	0.39	.....	.....	0.13	0.39	2.25	3.25	2.00	4.60	12.73	14.47	10.76
Taylor, Ky.	.....	3.25	0.56	1.28	1.61	21.65	4.51	9 31	0.54	7.58	4.51	4.20	8.61	27.05	24.83	20.06
Travis, Texas	0.94	11.11	13.33	8.98	.....	36.30	30.08	23.71	0.47	2.22	6.47	3.22	21.05	125.18	359.10	177.65
Upton, N. Y.	.....	.....	1.27	0.45	.....	.....	.....	.....	.....	0.49	.....	0.15	0.43	1.96	23.34	8.93
Totals	0.62	2.36	2.77	1.91	0.65	6.71	4.28	3.94	1.17	2.84	5.79	3.33	9.61	31.67	85.69	43.39

because soldiers in those camps were born in more crowded states than those whence they were recruited (see below).

The relation of the total epidemic diseases in camps to nativity is well brought out in Figure 8. This map combines admissions from primary lobar pneumonia; measles, simple or complicated; cerebrospinal meningitis and German measles. The sum of these admissions for the natives of each state is divided by the total admissions for the corresponding state of nativity. The total, then, shows for the dif-

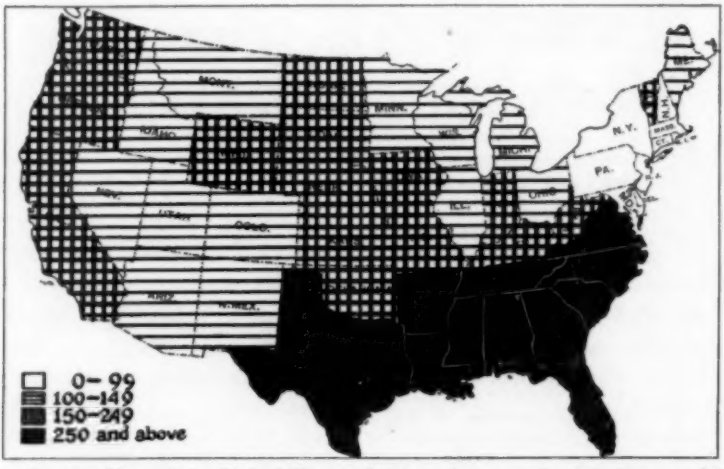

Fig. 8.—Map of the United States showing the sum of admissions to sick report for primary lobar pneumonia; measles, simple or complicated; cerebrospinal meningitis and German measles. The chart gives for the different states the relative proportion of admissions to sick report which were for the named epidemic diseases. The table is drawn up by dividing the number of admissions in 1917 of the given diseases by nativity × 1,000 (Table 60, S. G. Rep., 1917) by total admissions by nativity (Table 10, S. G. Rep., 1917).

ferent states the relative proportion of admissions to sick report which were for the named epidemic diseases. The consistently high proportion in the Gulf and South Atlantic States is striking. The southern Central States and the great prairie region west of the Mississippi River, and the Pacific States come next; the densely populated New England States, the Middle States and Maryland, have the least.

Just why the sparsely settled states of the Great Basin showed such a small amount of infectious disease is a little doubtful. The most reasonable explanation is that a large proportion of natives were really born in more densely populated states. That this is so is shown by a little figuring. Assuming that the place of birth is given correctly, then we have a curious result. For the men of the draft age were

children approximately of 5 to 14 years of age at the time of the census of 1900 — 17 years of age before the draft. According to that census there were 243,500 such children in Wisconsin. The admission to sick report of natives of Wisconsin in 1917 was 10,700, or 4.4 per cent. of the children of Wisconsin in 1900. Similarly, the admissions to sick of natives of Tennessee was 6 per cent. of the number of children in that state in 1900. These two states are those of relatively stable population during the last seventeen years. In contrast to them we have in Oklahoma in the year 1900, 51,000 children and in 1917 an admission to sick report of 5,793 "natives" from that state, or 11.4 per cent. Now, Oklahoma is the state that has shown the greatest growth in the last seventeen years, and this has the greatest ratio of "natives" who were sick to actual natives of military age. This suggests strongly that many early immigrants to Oklahoma were classified at camp hospitals as natives of the state. They probably came from sparsely settled farming districts and so had the slight immunity represented by the chart.

Much the same confusion between nativity and early migration is found in the camp returns as to the nativity of the sick assigned to the states of the Great Basin. For we find in all of these states an abnormally high proportion of admissions to sick report divided by children from 5 to 14 years living in those states in 1910. Thus, for Arizona this proportion is 11.4 per cent.; in Utah, 11.1 per cent.; in Nevada, 10.6 per cent.; in Idaho, 11.5 per cent., and in Montana, 10.7 per cent. The reason why these rates are approximately double the rates of Wisconsin and Tennessee is that many of the men called natives of these states were merely early migrants to these states. They were not really born in them, but probably in some more densely populated states where they passed their early years and in which they secured a childhood immunity.

2. HYPOTHESES

1.—To explain the relation between immunity from disease and density of settlement of the territory in which troops were born, there are four hypotheses that come to mind and which deserve to be tested. The first hypothesis is that the recruits coming from densely populated areas are immune from a given disease because they have already had the disease. This hypothesis was formulated by Surgeon-General Gorgas when he visited Camp Wheeler at the height of the epidemic of measles on Nov. 26, 1917. He said: "I think the reason for the measles affecting so severely this particular camp is the fact that the men came from the surrounding southern states which are sparsely settled, and, therefore, the inhabitants do not, as a rule, have measles

in childhood." On this hypothesis the cause of immunity is the antecedent incidence in the soldiers of the specific diseases — measles, mumps, lobar pneumonia, cerebrospinal meningitis and scarlet fever, as the case may be.

The foregoing hypothesis encounters certain difficulties. At least, it is hardly feasible to regard it as sufficient to cover all of the cases of communicable diseases. Thus, the distribution of lobar pneumonia by state of nativity resembles closely, as we have seen, the distribution of measles and mumps. That is, in all cases the southern New England and Middle States are relatively immune and the Gulf States are relatively susceptible. Yet one cannot explain this distribution of immunity in the case of lobar pneumonia on the hypothesis that the immune persons had already had pneumonia during their early life. Lobar pneumonia is not a sufficiently frequent cause of morbidity in childhood and youth to warrant such a conclusion. As Table 7 shows, the rate of mortality from lobar pneumonia is relatively low throughout childhood and slightly lower in urban than in rural districts. Similarly, the states that show immunity from measles and mumps likewise show immunity to cerebrospinal meningitis, and contrarywise, the Gulf and South Atlantic States are susceptible. But, again, cerebrospinal meningitis is hardly so frequent a disease of early life as to warrant us in saying that the soldiers from the immune areas had acquired immunity to the disease by having had it in their youth. While it is true that measles (as measured by mortality) is much commoner during childhood in urban than in rural states, yet this is not true of scarlet fever, lobar pneumonia and meningitis. These facts are brought out in Table 11, taken from the census "Morbidity Statistics" from 1913 to 1916 consolidated.

TABLE 11.—"MORTALITY STATISTICS" FROM CIVIL POPULATION, U. S. CENSUS, 1913 TO 1916. PROPORTION OF PERSONS WHO DIED FROM CERTAIN DISEASES UNDER TEN YEARS OF AGE TO TOTAL DEATHS FROM THE DISEASE

Disease	Urban States	Rural States
Measles	0.960	0.740
Scarlet fever	0.824	0.844
Lobar pneumonia	0.187	0.202
Meningitis	0.060	0.754

Consequently, while the hypothesis of immunity through incidence of the disease in early years applies to measles and mumps, it does not apply generally.

2. A second hypothesis is that there has been a selective elimination of susceptible individuals in the more densely populated regions and that in the less densely populated regions this selective elimination

has been less rigid. On this hypothesis recruits coming from the larger cities and the densely settled states differ in their constitution from those coming from the rural districts and the less dense populated states, in that the susceptibles have been more largely eliminated by death. Consequently, they constitute a more resistent population than do recruits from the sparsely settled states.

The foregoing hypothesis cannot, however, be applied generally; if, indeed, it has any validity at all. In the first place, certain of the diseases to which the men from the New England and Middle States showed greatest immunity are not more apt to kill children in cities than in rural districts. This is true, for example, in the case of cerebrospinal meningitis, the epidemics of which are quite as apt to occur in small towns and villages as in larger cities (see Table 10). Again, although there is clear resistance to mumps in soldiers from the Northeastern States, still mumps rarely kills children and hence cannot act by selective annihilation to diminish the susceptibility of the population.

3.—A third hypothesis which has been suggested is that certain diseases which are widespread throughout the South, like malaria, hookworm, pellagra and intestinal parasites have increased susceptibility. This would account for the relatively small morbidity among troops from the sparsely settled states of the Central Basin, but would not account for the higher morbidity of the Northern States west, as compared with those east, of the Alleghenies. Also, we have no experimental evidence that such diseases increase susceptibility to measles, mumps, scarlet fever and the others.

4.—A fourth hypothesis is that recruits coming from large cities and other densely populated areas have acquired a general immunity to infectious or communicable diseases. This hypothesis assumes that any one of the communicable diseases leaves the body in a state of heightened resistance to all micro-parasites, possibly through a condition of persistent hyperleukocytosis. This hypothesis has, indeed, received scientific standing through the researches of Jobling[1] and others. If this hypothesis is valid, we should expect to find that resistance to communicable diseases runs fairly parallel with the density of population or of the living conditions in which persons are found.

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1. Jobling, J. W., and Petersen, W.: The Nonspecific Factors in the Treatment of Disease, J. A. M. A. **66**:1753, June 3, 1916.

2. Jobling, J. W.: The Influence of Nonspecific Substances on Infections, Arch. Int. Med. **19**:1042, June, 1917.

The history of epidemics is of interest in this connection. Thus, in the large epidemic of poliomyelitis in New York City in 1916, it was found that the densely populated areas of Manhattan showed a lower incidence than the less densely populated areas of Brooklyn and Queens. Thus the rates per 100,000 population were, in Manhattan, 125; in Brooklyn, 246; in Queens 318.[3] It is true that poliomyelitis was constantly present in preceding years and that the rate was, in these earlier years, higher in Manhattan and Bronx than in Brooklyn and Queens; but the rate was a small one, less than 2 per 100,000 on

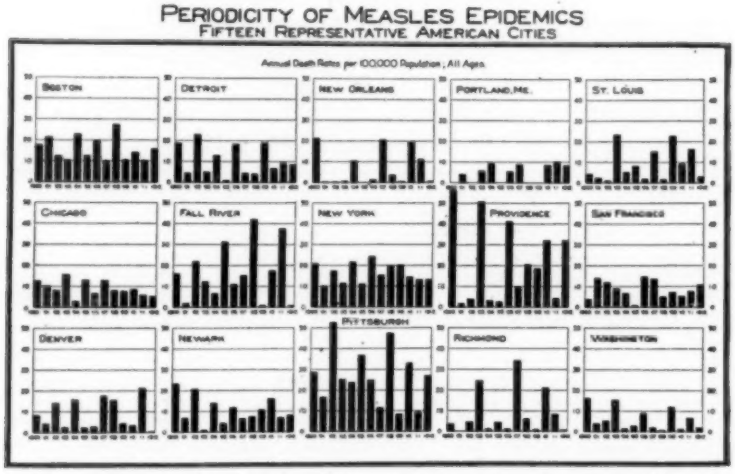

Fig. 9.—Graph showing for fifteen representative American cities the periodicity of epidemics of measles (furnished by the Prudential Life Insurance Company).

the average for the less sparsely populated burroughs; less than 5 per 100,000 on the average for the more densely populated burroughs. These low rates were clearly not sufficient to cause the difference in immunity to the great epidemic between Manhattan on the one hand and Queens on the other.

It has, indeed, been shown, as result of studies made by the New York City Department of Health,[4] that the Russian and Austrian population of that city, living under the most crowded and unhygienic conditions, are most resistent to the various diseases of infancy, so that they have a relatively low mortality.

3. Monthly Bulletin California State Board of Health, January, 1919, p. 227.

4. Guilfoy, W. H.: The Influence of Nationality upon the Mortality of a Community, Department of Health of the City of New York, Monograph No. 18, November, 1917.

Another phenomenon which speaks for the conclusion that "non-specific therapy" has given a general immunity for epidemics is found in the history of epidemics. It is a common experience that after an

TABLE 12.—Death Rates per 100,000 of Population in Registration Cities. From "Mortality Statistics," United States Bureau of the Census, 1912-1916

	Measles	Scarlet Fever	Whooping Cough	Total		Measles	Scarlet Fever	Whooping Cough	Total
District of Columbia:					**Birmingham, Ala.:**				
1912	1.6	1.6	8.6	11.8	1912	13.2	2.2	9.9	25.3
1913	7.7	5.2	1.2	14.1	1913	7.3	1.0	16.7	25.0
1914	....	0.4	2.4	2.8	1914	11.9	6.0	19.9	37.8
1915	2.3	3.1	3.1	8.5	1915	5.5	20.2	0.9	26.6
1916	1.9	1.9	4.9	8.7	1916	....	1.8	1.8	3.6
Omaha, Neb.:					**Bridgeport, Conn.:**				
1912	0.8	3.9	14.0	18.7	1912	6.4	17.4	9.2	33.0
1913	0.8	10.7	2.3	13.8	1913	13.4	26.8	7.1	47.3
1914	1.5	12.8	7.5	21.8	1914	28.6	16.5	18.2	63.3
1915	8.0	14.1	10.4	32.5	1915	6.8	7.6	19.4	33.8
1916	1.8	33.8	1.8	37.4	1916	15.6	3.3	12.3	31.2
Atlanta, Ga.:					**Springfield, Ill.:**				
1912	9.9	1.8	4.5	16.2	1912	5.5	....	14.6	20.1
1913	6.1	....	10.4	16.5	1913	31.9	1.8	24.8	58.5
1914	10.1	0.8	8.4	19.3	1914	....	9.2	7.3	16.5
1915	1.6	0.8	8.7	11.1	1915	3.9	10.7	1.8	16.4
1916	0.8	1.5	2.3	4.6	1916	8.9	6.5	16.4	31.8
Fall River, Mass.:					**Richmond, Va.:**				
1912	1.6	7.3	4.9	13.8	1912	1.2	....	2.4	3.6
1913	58.9	21.8	11.3	92.0	1913	19.0	4.7	8.3	32.0
1914	2.4	9.6	17.5	29.5	1914	1.2	2.3	21.1	24.6
1915	14.2	4.7	21.3	40.2	1915	....	1.0	....	1.0
1916	30.4	1.6	13.2	45.2	1916	15.9	3.0	13.9	32.8
Los Angeles, Calif.:					**New Haven, Conn.:**				
1912	0.3	2.2	9.8	12.3	1912	18.7	5.7	12.9	46.3
1913	13.7	3.3	6.3	23.3	1913	1.4	8.5	7.8	17.7
1914	1.4	1.2	2.6	5.2	1914	21.5	4.8	4.8	31.1
1915	4.2	2.2	2.0	8.4	1915	12.2	3.4	6.8	22.4
1916	1.9	1.4	9.3	16.1	1916	5.3	6.7	12.7	24.7
Minneapolis, Minn.:					**Jersey City, N. J.:**				
1912	3.4	4.6	2.8	10.8	1912	5.3	9.2	12.8	27.3
1913	6.0	18.6	4.5	29.1	1913	10.4	14.3	12.9	37.6
1914	2.6	26.1	12.8	41.5	1914	4.4	7.5	4.1	16.0
1915	3.7	3.1	4.8	11.6	1915	17.7	5.0	13.0	35.7
1916	20.4	4.4	7.4	32.2	1916	5.9	3.9	5.2	15.0
Oakland, Calif.:					**New Haven, Conn.:**				
1912	3.0	....	9.6	12.6	1912	18.7	5.7	12.9	37.3
1913	....	1.1	1.1	1.2	1913	1.4	8.5	7.8	17.7
1914	15.6	2.9	14.5	33.0	1914	21.5	4.8	4.8	31.1
1915	2.6	0.5	10.0	13.1	1915	12.2	3.4	6.8	22.4
1916	....	....	2.5	2.5	1916	5.3	6.7	12.7	24.7
Pittsburgh, Pa.:					**Waterbury, Conn.:**				
1912	27.7	11.1	10.3	49.1	1912	9.0	7.7	2.6	19.3
1913	27.9	29.1	14.5	71.5	1913	17.4	3.7	13.7	34.8
1914	9.1	34.4	7.8	51.3	1914	3.6	17.0	7.3	27.9
1915	13.0	9.7	7.7	30.4	1915	7.1	....	11.8	18.9
1916	23.4	3.8	16.7	43.9	1916	13.8	....	5.7	19.5
San Francisco, Calif.:									
1912	11.3	0.7	5.3	17.3					
1913	1.9	4.3	3.8	10.0					
1914	10.7	1.2	12.5	24.4					
1915	5.0	1.8	4.8	11.6					
1916	1.3	1.6	3.8	6.7					

epidemic year communities will be exceptionally free from epidemics for a year or two later. This result is illustrated in the chart (Fig. 9, furnished by the Prudential Insurance Company) of annual death rates from measles per 100,000 of the population of fifteen representative

cities. It is seen that great maximums (as at New Orleans, Fall River, Providence and Richmond) are followed by minimums in the next year. The large cities (New York, Chicago, Boston and St. Louis) show less extreme fluctuations, because such cities are really groups of cities, and the epidemic does not spread over all of the territory included in them during a single year.

This periodicity in the recurrence of epidemics is generally explained on the hypothesis that all persons susceptible to the particular epidemic diseases have acquired that disease during the first year of the epidemic. But this is not the whole story. For not only is the disease which became epidemic uncommonly scarce in the following year, but also some other epidemic diseases. Thus, if the mortality from measles, scarlet fever and whooping cough in cities from 50 to 250,000 inhabitants be studied in successive years, it will be found a common, if not the usual, event that the year following an epidemic of measles will be one of exceptionally small mortality for whooping cough or scarlet fever.

Data for this study have been obtained from the mortality statistics, Table 3, of the United States Bureau of the Census, years 1912 to 1916 inclusive. The results from certain selected cities are tabulated in Table 12. The mortality curve for all these diseases combined tends to crawl up to a maximum and then fall suddenly in one year (or sometimes two) to a minimum and then gradually in successive years to advance to a new maximum (Fig. 10). Thus, in Figure 10 we see that the great epidemic of measles in Bridgeport in 1914 was followed in 1915 by a minimum, not only of measles, but also of scarlet fever (1915 to 1916). In Fall River the measles epidemic of 1913 was followed by a minimum of measles in 1914, and a declining rate in scarlet fever. The whooping cough maximum comes two years later. In Atlanta, Ga., Los Angeles, Calif., and Springfield, Ill., there is a similar history.

A similar result appears in the history of epidemics in our army camps. German measles replaced common measles in Camp Lewis during the autumn of 1917. An epidemic of measles, like that of 1917, was anticipated in the autumn of 1918. The camps contained new recruits among whom was much susceptible material. Measles was present, as well as mumps, scarlet fever and cerebrospinal meningitis, yet they did not spread. There were fewer admissions on account of measles in the camps during the week ending Oct. 11, 1918, when the influenza epidemic was at its height, than during the summer week ending August 30. Some meningitis appeared as the crisis of the influenza was passing — and this may be regarded as a complication

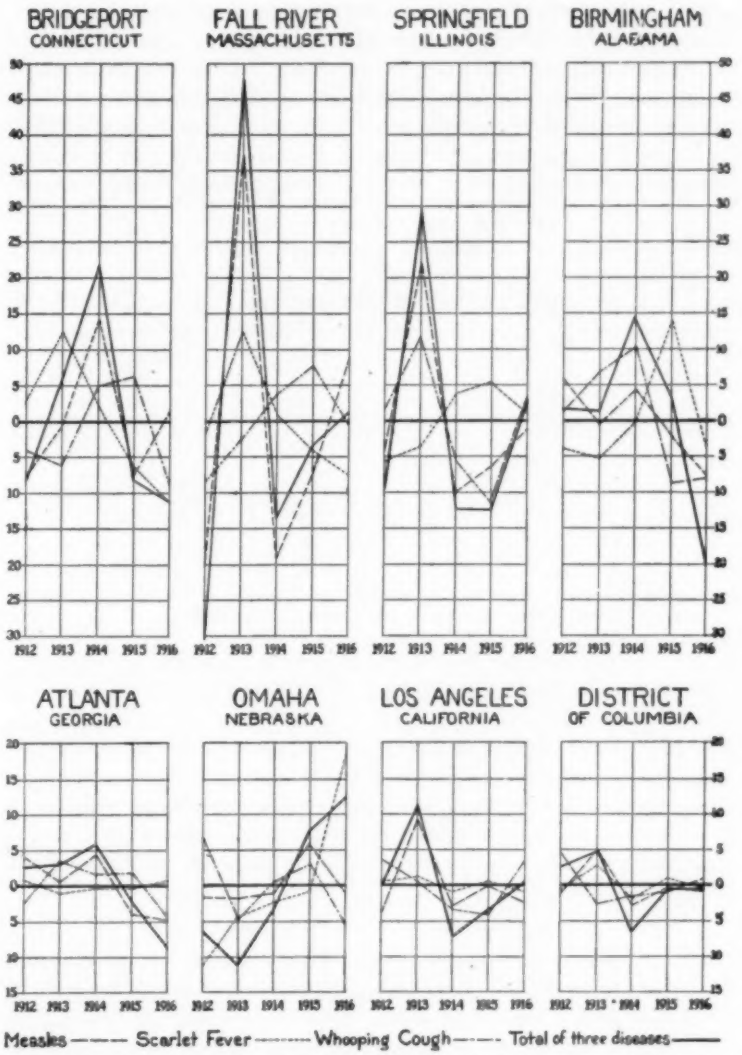

Fig. 10.—Graphs showing for eight cities the deviations in mortality rate from the average mortality rate for the years 1912 to 1916, inclusive. Curves are given for measles, scarlet fever, whooping cough and the sum of mortality from these three diseases.

of the influenza — but it never became epidemic. In Camp Hancock alone (in November) was there any important outbreak of scarlet fever. While the influenza pandemic was active and afterward (except for complications of influenza), the morbidity from contagious disease at the camps was rather low. This is indicated by the following table, based on the weekly telegraphic reports to the surgeon-general's office.

TABLE 13.—Comparison of Sickness in Camps from Measles, Meningitis and Scarlet Fever During November, 1917, and 1918 (Annual Rate per 1,000 for Special Diseases)

Disease	1917			1918	
	Week Ending	National Guard	National Army	Divisional Camps Week Ending	
Measles.....	Nov. 2	151	98	Nov. 1	18
	9	451	164	8	28
	23*	534	167	22	40
	30	300	123	29	35
	Dec. 7	308	163	Dec. 6	31
Meningitis.....	Nov. 2	0.4	2.7	Nov. 1	3.3
	9	1.1	2.9	8	1.6
	23	2.7	5.6	22	1.0
	30	3.8	3.2	29	0.4
	Dec. 7	5.4	4.1	Dec. 6	0.7
Scarlet fever....	Nov. 2	2.8	0.7	Nov. 1	1.0
	9	1.4	0.7	8	10.0
	23	2.1	3.6	22	19.4
	30	1.6	9.5	29	8.3
	Dec. 7	1.1	9.7	Dec. 6	1.8

* Report for week ending November 16 not available at this writing.

The extraordinarily low rate for measles in 1918 is sufficiently evident; that for meningitis, though less striking, is none the less real. The rate for scarlet fever was temporarily raised in November (9 to 23), 1918, by conditions at Camp Hancock, otherwise the number of cases of scarlet fever in camps was small.

In view of the foregoing facts, the fourth hypothesis formulated above should be kept in mind as a possible explanation of the high resistance shown by troops coming from the more densely settled parts of our country.

SUMMARY OF CONCLUSIONS

1. In mobilization camps, communicable diseases have produced the least admission and death rate in those camps which drew from areas that were prevailingly urban. The highest morbidity and mortality rates have been from camps that drew from the sparsely populated areas of the Southern Atlantic and Gulf States, and to a less striking extent from the sparsely settled states of the West.

2. The foregoing conclusion is based upon the studies made of measles, mumps, lobar pneumonia, cerebrospinal meningitis, scarlet fever and influenza.

3. The commonest explanation of this relation is that recruits from prevailingly urban territory had acquired immunity through having had the disease in their youth. This hypothesis does not cover the case of the rarer diseases of childhood, such as cerebrospinal meningitis.

4. Another hypothesis is that the immunity is due to a selective elimination of susceptibles. It is assumed to be greater in densely populated than sparsely populated areas. This hypothesis fails, however, to account for immunity in the case of mumps which does not kill children.

5. Another hypothesis is that life in urban communities produces a general resistance to disease of which the observed resistance to measles, mumps, lobar pneumonia, cerebrospinal meningitis, scarlet fever are only special instances. Many collateral facts speak strongly for this hypothesis.

PATHOLOGIC ANATOMY AND BACTERIOLOGY OF INFLUENZA *

EPIDEMIC OF AUTUMN, 1918

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In this paper the results of our studies on the pathologic anatomy and bacteriology of influenza during the epidemic of the fall of 1918 at Camp Zachary Taylor and Camp Knox, Kentucky, are presented.

Necropsies, with routine bacteriologic cultures, were performed throughout the entire epidemic, so that a fairly definite picture of its various stages could be formed. The present investigation has been limited to 126 definitely proven fatal cases of influenza. These were selected from a considerably larger number by ruling out all patients who clinically gave evidence of preexisting disease, such as tuberculosis, measles, etc., or where such evidence was found at the necropsies. Thus the morbid changes encountered may be looked on as primarily representing the end-results of the virus of influenza and its commensals.

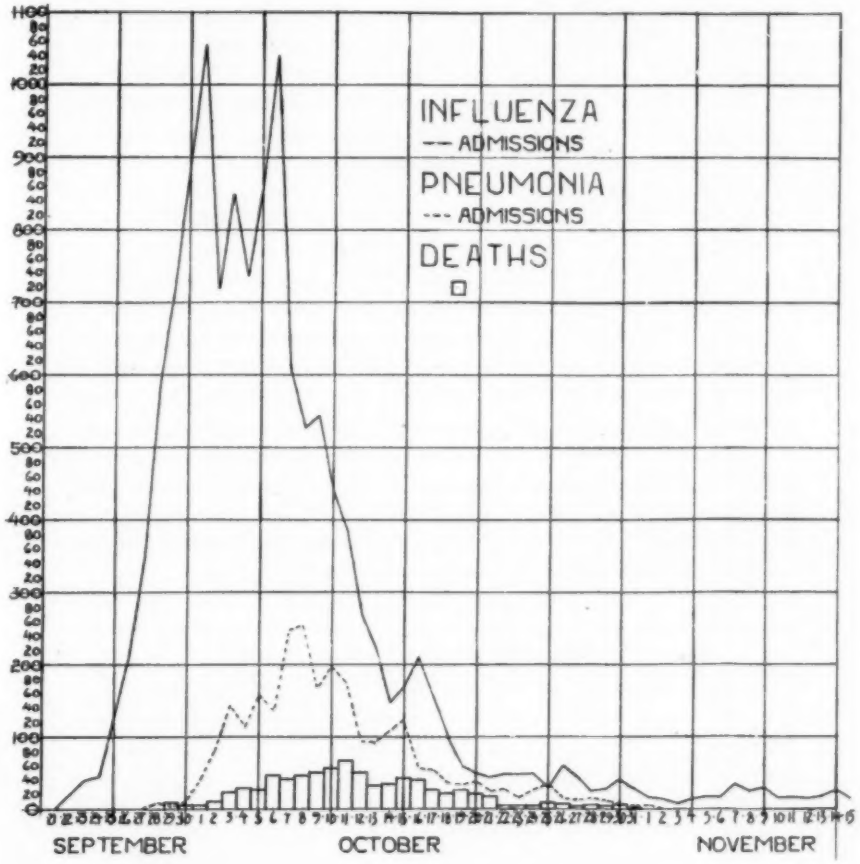
No attempt has been made to give even a nearly complete bibliography, but for the purpose of comparison a limited number of references are cited. A great aid in this has been the exhaustive monograph of Leichtenstern-Sticker,[1] which deals with the pandemic of 1889 and the succeeding years. However, the original sources, as far as possible, have been consulted, since the monograph cited is primarily clinical. The work of Kuskow,[2] who studied forty undoubted cases of influenza in 1892, at Petrograd, deserves special mention, since it represents the most detailed anatomic work of that period. The present European epidemics have been summarized by the British

* From the Cantonment Laboratory, Base Hospital, Camp Zachary Taylor, Ky.

1. Leichtenstern, Otto: Influenza, Ed. 2, by George Sticker. Wien. u. Leipzig, Alfred Hoelder, 1912.

2. Kuskow, N.: Zur pathologischen Anatomie der Grippe, Virchow's Arch. **139**:406, 1895.

commission.[3] Most of the American literature is very recent and readily accessible, and for that reason only such quotations are made as apply more directly to the subject under discussion. An examination of the literature of both the present and the preceding pandemics will bring out that most writers have confined themselves to the dis-



ease changes in the respiratory tract, and that the disease seems to have varied greatly in virulence and its manifestations. The anatomic changes described at different times and places are often quite dis-

3. Abstracts of Foreign Literature Compiled by British Medical Research Committee, J. A. M. A. **71**:1573 (Nov. 9) 1918.

similar. On the other hand, it is noteworthy that Lubarsch[4] and Hansemann (Report of British Commission) comparing the organs preserved since the preceding epidemic with those obtained from recent fatal cases, insist on the essential similarity of the lesions.

Time of Epidemic.—The pandemic manifested itself here first, Sept. 22, 1918, reached its height October 31, slightly declined again, reaching an apex comparable to the first on October 5, and terminated about November 15. Since this time only a small number of cases have occurred.

The first death due to influenza occurred September 28. The death curve gradually rose, reaching its highest point (seventy cases) October 5, and then gradually declined. (Graph 1.)

MORBIDITY AND MORTALITY FROM INFLUENZA AMONG WHITES AND NEGROES

The average aggregate population of this camp and of Camp Knox during the influenza epidemic was 58,000. Of these, 5,500 were negroes. A considerable discrepancy in the morbidity and mortality rate was observed between the two races (Table 1.) The number of cases of influenza per 1,000 population was 231 for the whites and seventy for the negroes. The number of deaths per 1,000 population was sixteen for the whites and seven for the negroes, but the number of deaths per 100 cases of influenza was 6.8 for the whites and 10.2 for the negroes. It shows, then, that while the incidence of influenza was considerably less among the colored soldiers, the mortality among those that contracted the disease was considerably higher.

TABLE 1.—MORBIDITY AND MORTALITY FROM INFLUENZA AMONG WHITES AND NEGROES, SEPT. 22, 1918, TO DEC. 1, 1918

	Total	Whites	Negroes
Average population	58,597	53,031	5,566
Morbidity—			
Actual number of cases of influenza	12,640	12,249	391
Number cases of influenza per 1,000 population	216	231	70
Mortality—			
Actual number of fatal cases	871	831	40
Number of deaths per 100 cases of influenza	6.9	6.8	10.2
Number of deaths per 1,000 population	15	16	7

There are three possible explanations for this discrepancy: exposure to infection, immunity and anatomic differences. Exposure may be dismissed, since practically all men were equally exposed. Immunity does not seem to us to play any part here, since once the disease was

4. Lubarsch: Die Anatomischen Befunde, von 14 tödtlich verlaufenden Fällen von Grippe, Berl. klin. Wchnschr., **55**:771, 1918. (Quoted by British Commission.)

contracted the mortality among the colored race was higher. It was observed in this camp throughout the past two years that various acute respiratory infections, such as catarrh of the nasal sinuses, were relatively uncommon among the colored soldiers and the explanation seemed to be that the rarely obstructed upper air passages of the negro afforded a good defense against lodgment of micro-organisms. This would hold true, of course, only for the individuals with more pronounced African features, disappearing with increased admixture of white blood. Opie[5] and his co-workers found negroes only about half as frequently infected as whites.

DURATION OF DISEASE

Eight patients, or 6.7 per cent., died within the first 5 days; average duration, 4.3 days.

Forty-nine patients, or 40.8 per cent., died within 6 to 10 days; average duration, 8.2 days.

Thirty-one patients, or 25.8 per cent., died between 11 and 15 days; average duration, 12.8 days.

Thirteen patients, or 10.8 per cent., died between 16 and 20 days; average duration, 17.5 days.

Nineteen patients, or 15.8 per cent., died after 20 days; average duration, 25.3 days.

In one case the duration of the disease was not obtainable. The average duration for the entire series was fourteen days. Lyon[6] found the average duration of life in his fifty-six cases to be 12.4 days. In five cases the disease exceeded forty days in duration. These, however, were typical influenza patients and may be looked on as having suffered from the chronic form of this disease. We shall describe the anatomic and bacteriologic findings of these chronic cases in a separate part of this communication. Otherwise, all the statements made apply to the 121 cases of acute influenza.

The relation of the duration of the disease to the period of epidemic was estimated (Table 2). For this purpose the entire epidemic was divided into five periods, generally of ten days each, except the last, which comprises the more scattered forms occurring in November and December. The table shows that of the forty-two cases necropsied during the first ten days after the first death of influenza had occurred, the average duration of the disease was 10 days. In the second period,

5. Opie, Eugene L., Freeman, Allen W., Blake, Francis G., Small, James C., Rivers, Thomas M.: Pneumonia Following Influenza (Camp Pike, Ark.), J. A. M. A. **72**:557 (Feb. 22), 1919.

6. Lyon, M. W., Jr.: Gross Pathology of Epidemic Influenza at Walter Reed General Hospital, J. A. M. A. **72**:924 (March 29), 1919.

it rose to 13.6 days, in the third to 16.6, in the fourth to 16.7 days. In the fifth period it dropped to 13.1 days. This last period, as stated, comprises the time when the disease had lost more or less of its epidemic character. The difference in the duration of disease as the epidemic progressed is doubtless due to the fact that the most susceptible patients succumbed first, and that the least susceptible resisted a longer period. The duration of disease during the fifth period is more difficult to explain, but it may have been due to the incoming of non-exposed troops, or to fewer precautions taken by individuals because of the belief that the epidemic was over. Later we will show that the bacterial findings of this period approximated those of the earlier stages of the epidemic. It should also be remarked that at this time there occurred a particularly severe outbreak of the disease in the neighboring town of Louisville.

TABLE 2.—Relation of Duration of Disease to Period of Epidemic

	Duration of Disease										Total Number of Cases	Average Duration in Days
	1 to 5 Days		6 to 10 Days		11 to 15 Days		16 to 20 Days		More than 20 Days			
	No. of Cases	Average Duration in Days	No. of Cases	Average Duration in Days	No. of Cases	Average Duration in Days	No. of Cases	Average Duration in Days	No. of Cases	Average Duration in Days		
First period: Sept. 30 to Oct. 9	5	4.4	29	7.8	7	12.0	1	16.0	..	....	42	10.0
Second period: Oct. 10 to Oct. 19	2	4.5	10	8.2	12	13.8	5	17.6	1	24.0	30	13.6
Third period: Oct. 20 to Oct. 29	..	....	1	9.0	3	14.0	3	18.3	8	25.2	15	16.6
Fourth period: Oct. 30 to Nov. 9	..	....	1	9.0	5	12.0	1	18.0	6	27.8	13	16.7
Fith period: Nov. 10 to Dec. 26	1	4.0	8	7.3	4	12.0	3	18.0	4	24.2	20	13.1
Total and Aver.	8	4.3	49	8.2	31	12.8	13	17.5	19	25.3	120	14.0

PATHOLOGIC ANATOMY

The necropsies were performed under ideal conditions, usually within a few hours, only rarely later than twelve hours after death. The tissues were routinely preserved in Zenker's fluid, occasionally in liquor formaldehydi. Fresh material was sometimes used for the study of cloudy swelling. Tissues routinely sectioned were heart, lungs, peribronchial lymph nodes, spleen, suprarenal, kidney, liver and brain. As occasion demanded sections were taken from skin, subcutaneous tissues, muscles, aorta and vessels in general, thoracic duct, extrapulmonary bronchi, semilunar ganglia, ureter, prostate, bladder, testes,

tongue, tonsils, intestines, pancreas, mesenteric lymph nodes, pituitary gland and spinal cord. The stain used for the accompanying photomicrographs was the eosinmethylene blue combination.

The description of the structures will be given in the order in which they are usually examined here at the necropsy (modified Zenker-Letulle method).

External Appearance. — The average age was 25.21 years; the average weight 76 kg.; the average height 174 cm. No great variations from these figures occurred. Emaciation was observed only in the more protracted cases. The postmortem lividity was generally most extensive. The face as well as almost the entire body was of a dusky color, sometimes even purplish black. In about two-thirds of the cases a bloody, sometimes frothy discharge exuded from the nostrils and from the mouth. There was no marked variation from the standard of cadaveric rigidity, but there seemed to be a tendency for it to be somewhat delayed. The superficial glands were never found palpably enlarged. Edema, although always looked for, was never present, and this should be emphasized in view of considerable kidney changes to be described below. The joints were never enlarged, nor was any arthritic condition demonstrated at necropsy, although it was sometimes seen clinically.

The chest was frequently considerably expanded, often unequally, This is no doubt due to the marked compensatory inflation of the lung and the pleuritic effusions. Scaphoid abdomen has been described (Kuskow[2]). This is probably coincidental and did not occur here, excepting in isolated cases.

Skin.—Various skin lesions have been described. Of these, the ones mentioned most frequently are exanthemata, resembling measles or scarlet fever; diffuse redness of the skin; sudamina and miliaria (Kuskow,[2] Leichtenstern[1]). Miliaria was very frequent and due to the profuse sweating (grippe sudorale). Such conditions as urticaria and psoriasis mentioned in connection with influenza are probably coincidental. In our series two cutaneous lesions occurred in a large number of cases. In about 20 per cent. of our patients there were multiple petechial hemorrhages in the form of minute, dusky, blue black areas, varying in diameter from 1 to 3 mm., and being most frequently met with in the axilla and over the scapula, although occasionally seen elsewhere. Because of the intense postmortem lividity they were recognized with difficulty. Microscopically (Fig. 1), small hemorrhages (up to the size of a low power microscopic field), were seen in the papillary layer of the skin, a papillary projection being often entirely flooded with red cells and only occasionally were these

hemorrhages seen in the deeper layers. These extremely superficial hemorrhages may be looked on as resembling the purpura hemorrhagica of influenza (Pick,[7] Drasche,[8] etc.).

The other skin lesions occurred in the form of small, discrete, slightly raised, red papules or vesicles with slightly turbid but rarely frankly purulent contents, in about 60 per cent. of this series. This condition was almost entirely confined to the sternal region. Microscopically, the sebaceous glands were hugely dilated and heavily infiltrated with polymorphonuclear cells; frequently they were entirely destroyed and replaced by a necrotic mass or a small abscess. Besides the polymorphonuclear cells, small round cells, with occasional plasma cells could be seen. The sweat glands were seldom involved. This condition did not seem to resemble acne nor the several forms of erythema multiforme described in relation to influenza (Krannhals,[9] Kuskow,[2] etc.). This we regard as a toxic necrosis of the sebaceous glands, produced, perhaps, by endothelial proliferation of its vessels, and analogous to the toxic acnitis of tuberculosis. Its characteristic site, over the sternal region, renders it unlikely that we are dealing with a simple acne.

In about 10 per cent. of our series jaundice was present. This was never very marked, and amounted to little more than a tinging of the sclera and skin. Blanton and Irons[10] found it nine times in 123 postmortems; the majority of these cases appeared late in the epidemic. Symmers[11] saw it in seven out of twenty necropsies.

Subcutaneous Tissues.—Kuskow mentions no general changes, but in most of our cases the tissue was grossly somewhat more moist and congested than normal. Microscopically, nothing further was noted. In three necropsies, and in another not included here, a generalized subcutaneous emphysema was present. No mention of this complication is made in the voluminous European literature on the preceding pandemic, and during the present it appears to have appeared but rarely. In this camp, including all the clinical cases, it occurred nine times, the incidence, therefore, being 0.07 per cent. It was always most pronounced over the upper anterior chest, the neck and the lower part of the face, but in several cases it was distributed over the entire body; in one instance the left side of the scrotum was hugely ballooned.

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7. Pick: Ueber Influenza, Verhandl. d. 22 Cong. f. inn. med., Wiesbaden, 1905.
8. Drasche: Influenza, Wien. med. Wchnschr., Nos. 10, 12, 17, 1890.
9. Krannhals, H.: Die Influenzaepidemie des Winters 1889-90 in Riga, St. Petersburg, 1891.
10. Blanton, Wyndham B., and Irons, E. E.: A Recent Epidemic of Acute Respiratory Infection at Camp Custer, Mich., J. A. M. A. **71**:1988 (Dec. 14) 1918.
11. Symmers, Douglas: Pathologic Similarity Between Pneumonia of Bubonic Plague and of Pandemic Influenza, J. A. M. A. **71**:1482 (Nov. 2) 1918.

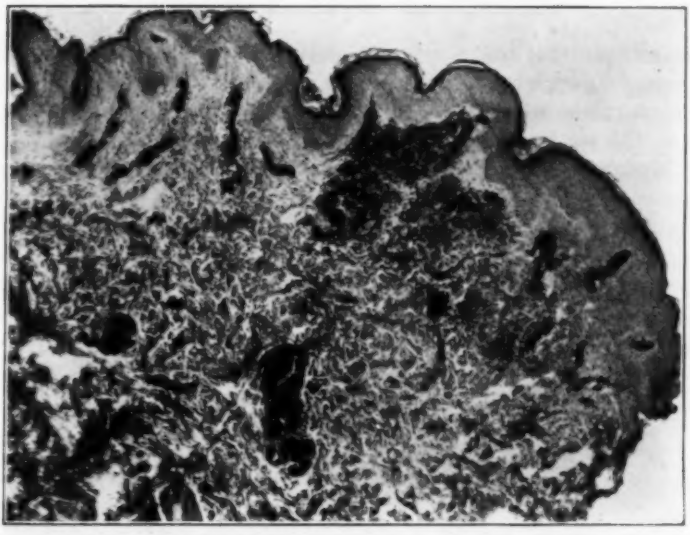

Fig. 1.—(Skin over upper chest.) Purpura hemorrhagica. Note dense hemorrhages in papillary layer of derma.

Fig. 2.—(Skin over chest.) Acute toxic necrosis of sebaceous gland. Note huge dilatation, cellular infiltration and necrosis.

The subcutaneous tissue appeared as if innumerable air bubbles were scattered throughout. The condition is being described in a separate communication where the details and the literature of the subject are given (Meyer and Lucke[12]). We need only say here that we found neither gross nor microscopic changes in the various organs which differed in any way from those of the rest of this series, with the exception that acute ulcerative bronchiectasis was more frequently noted here. We believe that the air escaping through the eroded bronchial wall was forced into the loose peribronchial areolar tissue and thence by line of least resistance gained the mediastinum and the subcutaneous tissue.

Fig. 3.—(Rectus muscle.) Coagulation necrosis (Zenker's hyaline degeneration), and early regeneration. Note swollen, evenly staining fibers, devoid of striations. In places clumps of nuclei denoting early regeneration may be seen.

Muscles.—In three instances considerable portions of the recti were of smooth, light reddish brown color, and had a peculiar, translucent appearance; in several more cases, about ten similar but smaller areas could be seen. This condition was confined to the abdominal muscles. Microscopically, typical Zenker's coagulation necrosis was met with (Fig. 3). This sometimes was present in only isolated fibers, but, in the three cases mentioned, extended over large areas. In one instance

12. Meyer, Jacob, and Lucke, Baldwin: Subcutaneous Emphysema, a Complication of Influenza, in Publication.

a marked acute myositis, with areas of necrosis and peripheral regeneration, was seen. Here dense masses of fibrin penetrated between the muscle fibers and into the structureless necrotic mass. Large numbers of round cells, polymorphonuclear cells and aggregations of muscle nuclei, in bundles and rows, were seen, especially at the periphery of the necrosed area (Fig. 4). Abscesses occurred in only one of this series, and in another instance among the cases of chronic influenza, although in the surgical wards, six abscesses of the rectus muscle were treated as complications of influenza. Rupture of the

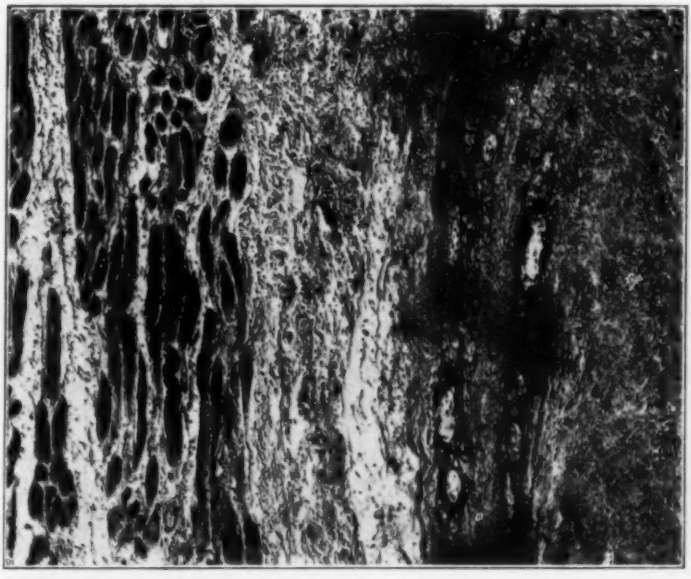

Fig. 4.—(Rectus muscle.) Acute suppurative myositis. Note partial necrosis, cellular infiltration and large amount of fibrin (right side of photograph).

rectus muscle and hemorrhagic exudations have been reported occasionally, but it did not occur in this series, although we have found it in noninfluenzal infections. Kuskow,[2] who saw several such hemorrhagic exudations in the muscles of the thorax and in the recti, believed it to be due to changes in the capillary walls, but also discusses the possibility of it being due to changes in the sympathetic nervous system. During the present European epidemic changes in the muscles seem to have occurred in from 10 to 20 per cent. of the cases (British Commission[3]). It must be said that the two most pronounced instances

of coagulation necrosis were present in conjunction with subcutaneous emphysema; this, however, is probably coincidental.

General Internal Inspection.—We mention here only in a general way the site of the abdominal organs, since this may be of some clinical interest. Usually the liver and the lower pole of the spleen extended well beyond the costal margins, due not only to a general increase in the size of these organs, but also to accumulations of pleural fluid, pressing them downward. The details of this and the external appearance of the other organs will be given under their respective headings.

TABLE 3.—Leukocyte Counts in a Number of Fatal Cases of Influenza

Necropsy Number	Duration of Disease, Days	Days before Death	Number of Leukocytes	Necropsy Number	Duration of Disease, Days	Days before Death	Number of Leukocytes
148	7	5	3,100	211	29	13	2,300
		3	2,100			7	8,700
		Day	2,900				
151	8	5	6,200	216	25	12	17,500
159	11	1	5,700	219	30	24	6,300
						7	10,000
160	12	9	10,200			14	13,600
		8	9,600				
		7	3,400	253	12	7	10,700
		5	8,600			6	10,100
						5	7,000
163	6	4	4,700			4	3,400
		3	7,800			3	3,800
		2	6,400			1	4,100
		1	8,000				
				258	29	9	11,100
165	8	3	7,000				
		2	12,200	262	45	30	8,400
		1	4,800			27	4,300
						24	11,000
170	15	7	4,300			17	10,000
		6	6,600				
		5	6,500	278	18	10	11,400
		4	8,400				
		3	11,000	280	24	4	17,600
						6	20,600
190	19	2	6,800				
				302	8	2	3,000
196	22	18	4,000				
		11	3,400	306	7	2	7,200
		6	10,000				
				316	11	6	4,300
201	24	17	4,000			4	6,400
		15	6,000			3	8,400
		14	3,000			2	9,700
		12	11,400				
		9	21,000	324	20	8	17,500
						3	20,200
206	28	6	5,000				

Peritoneum.—Peritonitis appears to be one of the rarest complications of influenza. Kuskow[2] collected the literature and found only eleven cases on record. Most of these coexisted with inflammations of other serous membranes, but some were thought to be primary by the writers. Blanton and Irons,[10] and Stone and Swift,[13] observed

13. Stone, Willard J., and Swift, George W.: Influenza and Influenzal Pneumonia at Fort Riley, Kan., J. A. M. A. **72**:487 (Feb. 15) 1919.

one acute case of peritonitis in 123 and 55 necropsies, respectively. In our series it occurred in none of the acute, and three times in the chronic cases, associated in every instance with pleuritis, and undoubtedly secondary to the pleural complication. The rarity of this condition is in striking contrast to the frequency with which it occurred during the measle-streptococcic epidemic of the preceding year.

The Blood Vascular System.—Blood Vascular Changes in General: In order to avoid repetition, certain general changes are enumerated here. Details, as they affect various structures, will be given in their proper place.

Grossly, there was an extreme congestion of practically all the structures of the body, the cut surface generally being excessively bloody. This was especially noticeable in the heart, kidneys, liver and brain. Microscopically, congestion and hemorrhages constitute ever recurrent findings. The capillary endothelium was frequently considerably proliferated, and the lumen of even good sized arterioles and venules was occluded with smooth, homogeneous, hyaline thrombi, or densely packed conglutination thrombi, consisting of degenerating red cells. Klebs[14] was the first to call attention to this condition, and believed vascular changes to be the primary and most important changes in influenza, and the catarrhal and inflammatory processes to be sequels of occlusion of capillaries. He described these capillary thrombi as consisting of granular degeneration products of red and white cells, occasioned by flagellated monads. (The flagellated organisms of Klebs and certain protozoa found here will be discussed in the bacteriologic part of this paper.) The occlusion of the capillaries occasions hyperemia of the neighboring parts, inflammations and exudations, and the deposition of pathogenic organisms which find in the thrombotic tissue a favorable medium. Klebs believed the cerebral symptoms and other functional changes in the nervous system to be due to these circulatory disturbances. We may say here that various other observers have been unable to confirm Klebs' view as to the importance of the flagellated protozoa. It may be, however, that the toxins producing the thrombi act further on the various tissues and that a combination of the vascular changes and bacterial activity bring about the anatomic alterations encountered in influenza.

The hyaline and conglutination thrombi have been experimentally studied by Flexner,[15] Pearce,[16] Simonds,[17] and others. Throughout the

14. Klebs, E.: Zentralbl. f. Bakteriol. u. Parasitenk. **7**:145, 1890; Deutsch. med. Wchnschr., Nos. 14 u. 16, 1890.

15. Flexner, Simon: J. M. Res. **8**:316, 1902.

16. Pearce, Richard: J. M. Res. **12**:329, 1904.

17. Simonds, J. P.: The Formation of Agglutination Thrombi in the Livers of Dogs after Injection with Witte's Peptone, J. Infect. Dis. **24**:297 (March) 1919.

tissues one frequently sees shadow erythrocytes denoting considerable blood destruction. The relative scarcity of polymorphonuclear leukocytes in the various tissues showing pathologic changes is striking, and gives one the impression that a myeloid intoxication exists here. A number of reports have given results of white blood counts and the consensus of opinion seems to be that a leukopenia is generally present. This occurred practically in all our clinical cases, and was looked on as one of our most important diagnostic aids. In Table 3 the counts of a number of the fatal cases are given. It will be seen that generally the leukopenia persisted throughout the disease, but that sometimes a slight leukocytosis occurred toward the end. In the

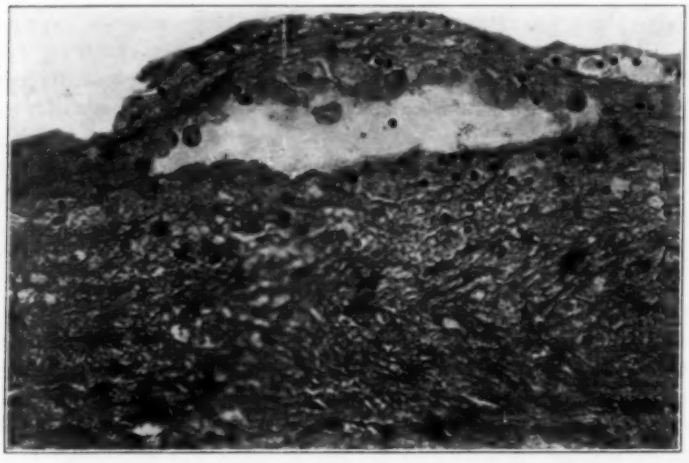

Fig. 5.—(Abdominal aorta.) Acute atheroma. Note slight bulging, cavitation and presence of huge, fatty degenerated cell. The most superficial layer of the intima is not affected.

cases where leukocytosis was present throughout, the pneumonic complications were of the croupous lobar type, or an associated purulent meningitis existed.

Aorta, Thoracic Duct and Vena Cava.—Definite subintimal changes, commonly looked on as the earliest manifestation of arteriosclerosis, were found in ninety-eight of a total of 120 cases in which a note was made on the condition of this vessel. The changes appeared as opaque, pale yellowish, or light orange yellow, narrow, firm streaks and corrugated ridges, generally occurring longitudinally on the posterior wall. The term "willow-tree branches," which has been applied to this condition, aptly describes it. Only exceptionally were hyaline plaques

found. The elasticity was never impaired, as tested in instances by a stretching apparatus. Generally, the entire length of the vessels presented these changes, but sometimes they seemed more marked in the ascending arch than in the abdominal aorta. Microscopically (Fig. 5), the endothelium was not affected. The more superficial layers of the intima were generally somewhat loosely arranged. The deepest layer was fibrous and swollen. At what appears to be a later stage the swelling is more pronounced. Very large cells with a ragged, granular, vacuolated, disintegrating cytoplasm were seen. Their nuclei were variable in their staining affinities and were often entirely absent.

Small, ragged walled cavities, bounded by the muscular wall and the most superficial layer of the intima were met with commonly. These, no doubt, were sometimes due to the dropping out of the degenerated cells during the process of sectioning, but are likewise the product of fatty and granular degeneration. A few scattered, small, round cells were found, but no definite infiltration. This early atheroma has been described by one of us (Lucke[18]) as frequently occurring in necropsies of measles patients. Karsner[19] found such changes in sixty-two out of eighty-one soldiers dying from endocarditis, and so forth, following war wounds, and in a large percentage of patients dying of various acute infections in this camp, this early aortic change was met with. A more detailed study of this finding is in progress.

The only other condition worthy of note was a diffuse hemoglobin tinting of the aorta and other great vessels. This occurred in many instances, even at necropsies performed within a few hours after death, and is probably a manifestation of rapid blood destruction. A mention of this condition is made by Le Count.[20] The vena cava and the other large vessels presented no gross alterations.

The thoracic duct, in every instance, was of normal diameter, thin walled, with a slightly pink mucosa. Neither gross nor microscopic changes were noted.

Pericardium.—Pericarditis was met with seven times; twice serofibrinous, on three occasions fibrinous, once fibrinopurulent, and once frankly purulent. Microscopically, the usual fibrinopolynuclear exudate was found. In each instance an associated pleuritis was probably the starting point of the inflammation. In approximately 20 per cent. of this series the pericardial fluid amounted to 50 or 60 c.c.; this, how-

18. Lucke, Baldwin: Postmortem Findings in Measles, Bronchopneumonia and Other Acute Infections, J. A. M. A. **70**:2006 (June 29) 1918.

19. Karsner, Howard T.: Acute Endocarditis Following War Wounds, Arch. Int. Med. **22**:296 (June) 1918.

20. LeCount, E. R.: The Pathological Anatomy of Influenzal Bronchopneumonia, J. A. M. A. **72**:650 (March 1) 1919.

ever, was most likely mechanical in origin, due to the pressure on the great veins by pleural exudate. Punctate, hemorrhagic extravasations were often seen over both the visceral and parietal pericardium, and in a majority of cases, definite hyperemia was present. Blanton and Irons[10] found serofibrinous pericarditis thrice in 123 necropsies; Kuskow,[2] five times in forty necropsies. From the literature (Kuskow[2]) it would seem that pericarditis is a rare complication of influenza, depending most likely on associated pleuritis.

Fig. 6.—(Heart.) Cloudy swelling and vacuolization. Note vacuoles in body of muscle cells (upper half of photograph), swelling of fibers, large oval nuclei and occasional chromatolysis.

Heart.—Contradictory reports are given in the literature. Symmers,[11] in twenty necropsies, found right-sided dilatation, congestion of capillaries and exceptionally cloudy swelling. Nuzum[21] and his co-workers, in forty necropsies, found the right heart acutely dilated. Stone and Swift,[13] in fifty-five necropsies, found right-sided dilatation in thirty-one instances, and dilatation of both sides in seven instances, and observed definite parenchymatous changes in the myocardium in many instances. No histologic examinations, however, were recorded.

21. Nuzum, John W., Pilot, Isadore, Stengle, F. H., and Bonar, B. E.: Pandemic Influenza and Pneumonia in a Large Civil Hospital, J. A. M. A. **71**:1562 (Nov. 9) 1918.

Ribbert,[22] and Birch-Hirschfeld[23] found no anatomic alterations. Wallis[24] and Kuskow[2] found acute parenchymatous inflammations as in other infectious diseases. We strongly support the opinion of the latter that the heart is always more or less affected and presents always certain alterations. The weight of the heart was estimated in detail in sixty-six cases (Table 7). In 30 per cent. of these it was below 300 grams, with an average of 267 grams. In 60 per cent. it averaged 364 grams, and in 10 per cent. it weighed 400 grams with an average of 429 grams. On the whole, the heart weight appeared increased, due probably more to congestion and edema than to actual hypertrophy. Lyon[6] found 322 grams the average in his series of fifty-six cases. In 115 cases of our series the right heart presented more or less dilatation, and in a number of instances the left side was likewise relaxed. In eighty-nine cases an associated cloudy swelling was diagnosed grossly. In the majority of instances, then, we encountered parenchymatous changes analogous to those seen in other acute infections.

The heart muscle was usually flaccid, sometimes excessively so. The cut surface practically was always opaque, grayish red, with fine lines due to capillary congestion. The characteristic tigroid markings of fatty degeneration were never seen. Microscopic examinations were conducted on both fresh and fixed preparations. As a rule, a granularity obscuring striations and clearing on the addition of acetic acid was found. In the stained preparation these changes were less clear, but here (Fig. 6) also one would frequently see haziness or disappearance of the cross striations, and very frequently, small vacuolization. Here and there the nuclei were pale and irregularly stained; many being swollen, oval, granular and fragmented. All these changes are similar to those seen in diphtheria and typhoid fever. In the interstitial tissue, occasionally, a few wandering cells, or a granular debris, were found. The intermuscular spaces were sometimes broad and contained a precipitated, granular mass, probably edematous in origin. The capillaries were often distended to an extreme degree; but very rarely small hemorrhages were seen. Conglutination and hyaline thrombi, spoken of above, were often seen, but not with the same frequency as in some of the other organs.

The endocardium, in a few instances, presented subendothelial, petechial hemorrhages of slight extent. The valve leaflets were involved

22. Ribbert: Anatomische und Bakteriologische Beobachtungen über Influenza, Deutsch. med. Wchnschr., No. 4, p. 15, 1890.
23. Birch-Hirschfeld: Schmidt's Jahrb., **226**:111, 1890.
24. Wallis, C.: Hygiea **70**: 1890 (cit. Schmidt's Jahrb., 1891).

only once, where acute vegetations were seen on the mitral valve. It would appear, from the literature, that endocarditis is one of the rare complications, and probably always secondary in origin.

Respiratory System.—Nares: The mucosa of the nares, especialiy in the cases early in the epidemic, was somewhat swollen, deep red and frequently exuded blood. No microscopic sections were made.

Accessory Nasal Sinuses.—These will be described here, rather than in the order of the necropsy. In sixty-five cases the accessory nasal sinuses were examined. In eight of them no gross alterations

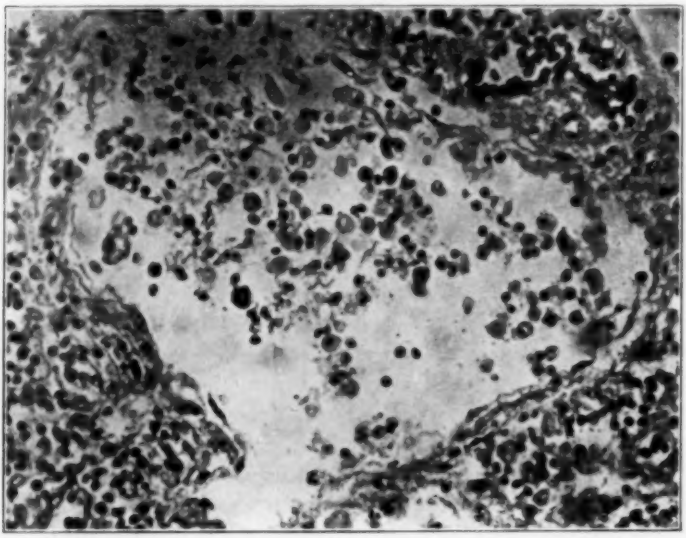

Fig. 7.—(Peribronchial lymph node.) Acute sinus catarrh. Note the widely distended lymph sinus and the presence of large mononuclear cells. The sinuses are generally more packed with cellular structures. This section was chosen to bring out the details.

were present. Generally, the mucosa was reddened, thickened, loose and the cavity contained a purulent or seropurulent material. Frequently this was heavily blood-stained, varying in consistency from a thin, watery, sanguineous exudate to a heavy, creamy, yellow, thick pus. The sphenoid sinus was involved fifty-one times, the ethmoid sinus forty-three times, the frontal sinus seventeen times, and the mastoid cells, on one or both sides, fourteen times. Stone and Swift,[13] in forty-one necropsies, found similar involvement in a large number of cases,

and Weichselbaum[25] and Drasche,[8] during the pandemic of 1889, saw similar changes. It would appear that the sphenoid sinus was the most frequently involved. Necrosis of the bone was never present, in marked contradistinction to the frequent and pronounced bone necrosis seen here during the measles outbreak of 1917-1918, even though at that time the accessory nasal sinuses were on the whole not so frequently affected as during the present pandemic.

Peribronchial Lymph Nodes.—In 115 cases congestion and edema of the peribronchial lymph nodes were grossly noted. In eleven cases no microscopic changes were demonstrable. The glands often attained

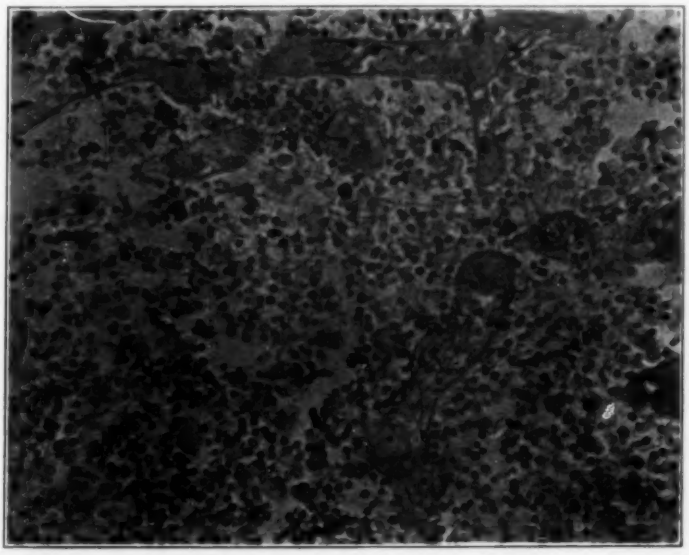

Fig. 8.—(Peribronchial lymph node.) Coagulation and fibrin thrombi. Note the densely packed and fused red cells, and strands of fibrin. Compare this with Figure 10 where the individual red cells are separate.

remarkable proportions, and it was not uncommon to see a mass the size of a walnut. Such excessive enlargement was present in thirty-two instances. The external appearance was generally a light reddish gray, occasionally a dark pinkish red. The consistency varied from mushy softness to flaccidity. The cut surface was practically always very moist, dripping blood stained fluid. The degree of congestion

25. Weichselbaum: Bakteriologische u. path.-anat. Untersuchungen über die Influenza u. Ihre Komplikationen, Wien. med. Wchnschr., No. 6, 1890.

varied, but the majority of cases were definitely congested, and, in some, tiny hemorrhages visible to the naked eye occurred. Microscopically, the lymph sinuses were widely distended and often packed with very large mononuclear, pale staining, phagocytic cells, containing bacteria and cell remnants (Fig. 7). Other sinuses showed a granular debris with delicate threads of fibrin, and, in some, dense accumulations of red cells were intermingled with the other constituents. Many cells resembled the phagocytic epithelial cells of the lung exudate. A number of camera lucida drawings of these cells made from both sources were compared and it seemed very probable that they belonged to the same group of elements. The lymphoid

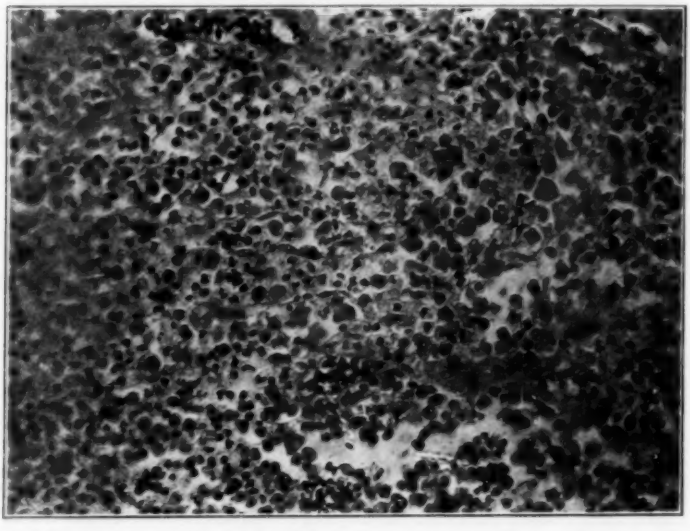

Fig. 9.—(Peribronchial lymph node.) Acute suppurative lymphadenitis. Note large numbers of polynuclear leukocytes throughout tissue. Note also the large mononuclear cells within the lymph sinuses and compare this with Figure 7.

tissue was generally loosely arranged, sometimes intermingled with a fine precipitate and occasionally fibrin. An active proliferation, as indicated by great numbers of large cells of the lymphoid type, appeared to be going on. Plasma cells occurred in considerable numbers in cases where the disease had persisted for some time.

The vessels throughout the glands were enormously congested, and now and then hemorrhagic foci were encountered. Almost in every instance some of the vessels contained smooth hyaline or conglutination, and, in a few cases, fibrin thrombi (Fig. 8). The vascular endo-

thelium was considerably swollen, the nuclei being often very large and the cytoplasm protruding into the lumen of the vessel. We believe that it is justifiable to look on the phagocytic cells in the lymph sinuses as of mixed origin. Part of them appear to be derivatives of vascular endothelium corresponding to the endothelial leukocytes that Mallory[26] has described. Others are probably epithelial, being carried to the lymph sinuses from the lung. These latter are differentiated by poorer staining, frequent vacuolization and other evidences of degeneration. On the whole, bacterial phagocytosis in the lymph node was rare. The perivascular spaces were packed with cells similar to those described, the relative absence of polynuclear elements being striking. In fact,

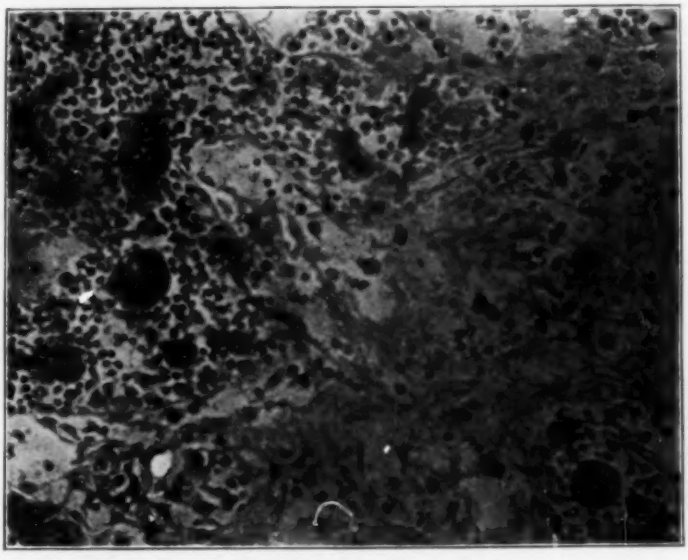

Fig. 10.—(Peribronchial lymph node.) Subacute productive lymphadenitis. Note the loosely arranged cellular young connective tissue. These changes are indicative of the fibrosis ultimately resulting.

these latter occurred only when the adjacent lung surface was covered with fibrinocellular exudate (Fig. 9). Now and then eosinophils, in inconspicuous numbers, were encountered. Occasionally the reticular fibrous tissue was actively proliferating, and large numbers of loosely arranged young connective tissue cells could be seen throughout the section. This subacute productive lymphadenitis occurred mainly in

26. Mallory, Frank B.: Principles of Pathologic Histology, Philadelphia, W. B. Saunders Co., 1914.

cases of some duration and appears to indicate the end-result of the process (Fig. 10).

To summarize the changes in the lymphatic glands: marked congestion and edema, acute sinus catarrh, frequent hyaline and conglutination thrombosis, and relative scarcity of polynuclear cells. Grossly, such changes have been described by Blanton and Irons,[10] Symmers,[11] Nuzum,[21] and others. Oberndorfer[27] examined some histologically and found enormous congestion, hemorrhages and proliferation of the endothelium, especially in the axillary glands.

Larynx.—The mucosa of the larynx was definitely reddened and somewhat swollen in only about one-third of our cases. Occasionally the glottis and surrounding structures were edematous, but ulcerations were never encountered. In a general way, the laryngeal mucosa was never as much involved as that of the lower trachea or the bronchi. This agrees with the observation of Drasche[8] and Oberndorfer. Leichtenstern describes several cases of hemorrhagic laryngitis, and B. Fraenkel[28] observed a laryngitis, with marked swelling and various degrees of redness, several times in association with a croupous exudate in thirty-three instances in his series of forty-five cases.

Trachea and Bronchi.—The mucosa of the trachea and principal bronchi was generally markedly reddened, cloudy and swollen, at other times it was of a paler red color and overlaid with mucopurulent or purulent secretions. The changes may be summarized as follows: The tracheitis and bronchitis were hemorrhagic in character sixty-three times, catarrhal thirty-one times, purulent twenty-three times, while in nine cases no gross alterations were noted. Hemorrhagic types were chiefly met in the more acute cases, the catarrhal and purulent forms occurring usually at later stages. Fibrinous exudates now and then covered a part of the tracheal or bronchial walls, but there were no distinct macroscopic ulcerations. Leichtenstern[1] believed that the inflammation was often most pronounced at the bifurcation, but this we cannot confirm. The contents of the tubes consisted usually of large amounts of frothy, blood stained material in the hemorrhagic types, while in the catarrhal and purulent forms great quantities of mucopus, or thick yellow, purulent fluid were found.

Several writers have drawn attention to the uneven distribution of the bronchial inflammation, considering this as one of the important complications of influenzal bronchitis (Kuskow,[2] Leichtenstern,[1] etc.). We can agree with their statements, for in our cases the alterations

27. Oberndorfer: Ueber die Pathologische anatomie der Influenza-artigen Epidemie, München. med. Wchnschr. **65**:810, 1918.
28. Fraenkel, B.: Deutsch. Wchnschr., No. 28, 1890.

were usually not uniform. Thus, the bronchi leading to diseased parts were usually more affected than those supplying healthy lung tissue. On the other hand, we have occasionally seen bronchial tubes intensely inflamed, while no marked changes in the surrounding lung tissue existed. The small bronchial branches presented generally the same changes as the larger tubes. Microscopically, most pronounced alterations were observed. Of these, desquamative bronchiolitis was the most frequent, the mucosa here being almost entirely destroyed. Ulcerative bronchiolitis was also very common. Sometimes the entire bronchial wall was eroded and replaced by a densely necrotic mass

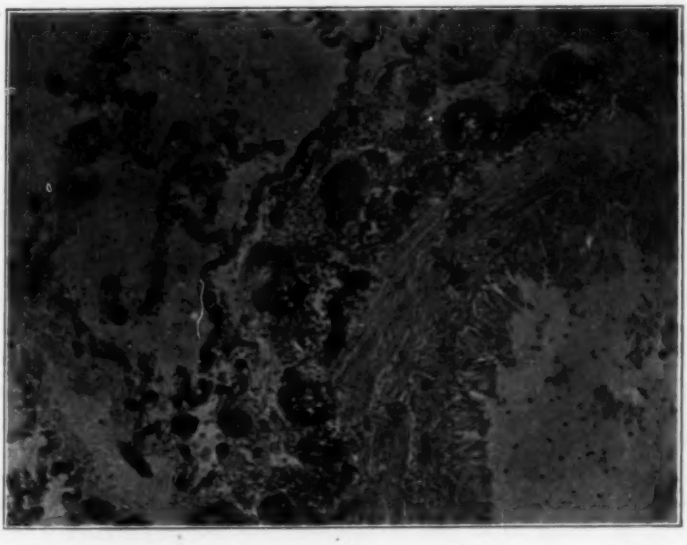

Fig. 11.—(Bronchus.) Acute hemorrhagic bronchitis. Note the dense congestion and small hemorrhages throughout the bronchial wall. The mucosa is partly necrotic but not as yet desquamated.

containing strands of fibrin and polymorphonuclear cells in various stages of degeneration. In the less affected bronchioles, and in the larger bronchial branches, extreme congestion and submucous hemorrhages were very general (Fig. 11). Thrombi of various natures, but usually hyalin, were common. The endothelium was often actively proliferated. Infiltration of the bronchial walls with polynuclear cells was frequent. The mucous glands usually presented mucoid degeneration. Bronchiectasis was relatively uncommon. Large ulcerations occurred in four instances only. This has been referred to above in connection with subcutaneous emphysema.

Pleurae.—The existence of pleuritis has varied greatly at different times and places. Thus, Symmers[11] emphasizes its infrequency, encountering it only thrice in twenty necropsies. Blanton and Irons,[10] in eighty of 123 necropsies; Hall, Stone and Simpson,[29] ten times in thirteen necropsies; Stone and Swift,[13] in thirty-one out of fifty-five necropsies; Nuzum and others,[21] practically always in forty necropsies. The majority of the above found it to be serofibrinous, and some lay stress on its serosanguineous character and its low fibrin content. During the preceding epidemic European writers found a similar discrepancy. Thus, Leichtenstern[1] saw seropurulent involvement twice in forty necropsies; Kundrat,[30] nine times in 126 necropsies; Mason,[31] in six of twenty-eight necropsies; Kelsch and Antony,[32] in nineteen out of 278 necropsies.

On the whole, the pleural involvement seems to have been less in the European pandemic of 1889 and succeeding years than in the present visitation. The discrepancy in the findings is probably not only due to the organism predominating in the various localities, but also to the period in an epidemic when the observations were made. Thus, our early cases presented far less pleural involvement than those occurring later in the epidemic. In each instance an associated pneumonitis was present. Primary pleuritis was never observed, although Kundrat emphasizes as one of the characteristics of influenzal bronchitis that it often leads to purulent pleuritis without accompanying pneumonia. It would appear, however, that no detailed microscopic studies were made by him or other writers who describe such a condition, and that their statements were based on macroscopic rather than on microscopic evidence.

In our series the pleura was involved on one or both sides in ninety cases. The exudate was sanguineous in twelve, fibrinous in twenty-seven, serofibrinous in nineteen, serofibrinopurulent in twenty-three, and frankly purulent in nine instances. The left pleura was somewhat more frequently involved than the right, the difference being as follows:

Exudate	Left Pleura	Right Pleura
Serosanguineous	6	8
Fibrinous	27	22
Serofibrinous	19	12
Seropurulent	21	19
Purulent	4	6

29. Hall, J. N., Stone, Murray, C., and Simpson, John C.: The Epidemic of Pneumonia Following Influenza at Camp Logan, Texas, J. A. M. A. **71**:1987 (Dec. 13) 1918.

30. Kundrat: Wien. klin. Wchnschr., 1890.

31. Mason: Boston M. & S. J., February, 1890.

32. Kelsch et Antony: LaGrippe dans l'armée Française en 1889-1890. Arch. de méd. et de pharm. milit., Paris **18**:1891. Kelsch: Traité des Maladies Epidémiques. Tome III. Paris, 1910.

It must be remembered that occasionally only one pleura was affected, and that, therefore, these figures differ from the consolidated incidence given above. The exudate was generally thin and apparently low in fibrin content. In the early part of the epidemic the serosanguineous types occurred most frequently, the fluid being definitely blood-tinged. Under fibrinous pleuritis are included all degrees of fibrinous exudation. Generally, only a small, fine, grayish, patchy deposit, often not more than a roughening of the pleura, was present. In the serofibrinous exudates small clumps of fibrin were floating in a relatively clear or only slightly turbid fluid. By serofibrinopurulent exudates are understood those fluids which were more definitely turbid. The purulent exudates were of the usual type. Analysis as to the amount of fluid could be made in seventy-one instances. The figures given apply to the fluid in either cavity. Thus, if both the right and left cavities contained a varying amount they were considered separately. Fluid was less than 100 c.c. in ten, between 100 and 500 c.c. in thirty-eight, between 500 and 1,000 c.c. in fifteen, between 1,000 and 2,000 c.c. in seven, and over 2,000 c.c. in one instance; the greatest number, therefore, containing less than 500 c.c.

Analysis in reference to the duration of the disease and period of the epidemic reveals the fact that the purulent and more pronouncedly fibrinous fluids occurred at a later stage of the disease or epidemic. Petechial hemorrhages were observed frequently, varying in extent, sometimes involving considerable areas and being in 50 per cent. associated with a pleuritis. Cytologically, the pleural exudate consisted chiefly of large mononuclear cells, with considerable numbers of polynuclear elements. Phagocytosis of bacteria was common. Microscopically, the pleura presented the usual changes encountered in exudative inflammations. The subserous vessels were generally hyperemic and frequently contained hyaline or conglutination thrombi.

Lungs.—The anatomic alterations of the lungs are usually the most pronounced and most striking. The question whether influenza is always accompanied by pneumonitis, or whether it is only one of the complications of this disease, has been much discussed, pro and con. Certainly, no matter what changes are present in the rest of the organs, pneumonic involvement is also encountered in the vast majority of instances. The widespread influenzal bronchitis prepares areas of lessened resistance for the secondary micro-organisms of the mouth and throat, which, in suitable environment, readily take on pathogenic properties and produce pneumonitis. It is this almost constant presence of a number of different organisms, each having its own special characteristics and producing its own special changes, which has led to the wide discrepancy in the reports of the anatomic changes. This is

perhaps more true of the lungs than of any other organ. It must always be remembered that the changes encountered are usually due to various secondary invaders of an already pathologic field, and while we shall attempt below to describe the alterations occurring in the lungs from which only one type of organisms was isolated, it seems best to first present the picture, regardless of the micro-organisms found in culture, for it is hardly possible to decide the exact extent for which this or that micro-organism was responsible. At all events it has been our impression that the chief characteristic of influenzal pneumonitis lies in the multiformity of lesions. Quotations from the literature have been especially limited here because of lack of space, but a very brief review is deemed necessary.

TABLE 4.—Duration of Influenzal Pneumonitis in Relation to Duration of Disease

Days Sick with Influenza	Duration of Pneumonia										Total Number of Cases	Average Duration in Days
	1 to 5 Days		6 to 10 Days		11 to 15 Days		16 to 20 Days		More than 20 Days			
	No. of Cases	Average Duration in Days	No. of Cases	Average Duration in Days	No. of Cases	Average Duration in Days	No. of Cases	Average Duration in Days	No. of Cases	Average Duration in Days		
1–5	8	2.75	....	.....	....	.....	....	.....	....	.....	8	2.75
6–10	29	3.79	14	6.86	....	.....	....	.....	....	.....	43	5.33
11–15	6	3.67	20	8.20	5	13.20	....	.....	....	.....	21	8.36
16–20	2	4.50	2	8.00	6	12.00	2	17.00	....	.....	12	10.38
Over 20	....	.....	1	9.00	3	14.00	8	17.08	3	26.00	15	16.06
Total and Aver.	45	3.68	37	8.02	14	13.07	10	17.32	3	26.00	100	

The usual form of influenzal pneumonitis has been described as lobular, the consolidations varying in size from very minute areas to entire lobes, and occurring almost as frequently in the upper as in the lower lobes. Such types have been described by Kelch and Antony,[22] Wallis,[24] Marchand,[33] Ribbert,[22] Kundrat,[30] Kuskow,[2] Drasche[8] and others. All of these authors describe the foci more or less differently. Thus, the cut surface was sometimes found smooth, at other times granular. The periphery was rarely sharply demarcated. The lung tissue was generally hyperemic, but sometimes it appears to have been definitely anemic. Consistency and color of these consolidated areas has varied so greatly that details cannot possibly be given. Purulent pneumonitis has been observed by Krannhals,[9] Kuskow,[2] Kundrat,[30] Drasche,[8] etc. Gangrene of the lung tissue has been found associated

33. Marchand: Berl. klin. Wchnschr., No. 33, 1890.

with this suppurative pneumonia, and has occasionally been found independently (Marchand,[32] Drasche,[8] A. Fraenkel,[34] Kundrat,[30] Kuskow[2]). Indurative pneumonitis has been observed by Drasche[8] and Kundrat.[30] True lobar pneumonia of the croupous type seems to have occurred with greater frequency during and after influenza than usually (Sokolowski,[35] Kundrat,[30] etc.). Noncroupous lobar pneumonia, or pseudolobar lobular pneumonia, has been so frequently encountered that it seems to be almost characteristic of this disease. The consolidated tissue here has an even, smooth cut surface and presents under the microscope an exudate, poor in fibrin and rich in catarrhal and polymorphonuclear cells (Gaescher,[36] Marchand,[33] L. Frank,[37] R. Simon,[38] etc.).

Microscopically, the exudate in the various forms has been found of every conceivable composition. Pfeiffer[39] found fibrin totally absent, or present only in small amounts. The cells were generally catarrhal or polymorphonuclear with frequent infiltration of the alveolar walls. He believed that influenzal pneumonia manifested itself first by peribronchial inflammation, which by coalescence formed larger lobar consolidations. Ribbert[22] found fibrin to vary greatly in amount, the cells being chiefly polymorphonuclears and desquamated epithelium with many red cells. Klebs[14] found fibrin constantly present and large numbers of red cells; polymorphonuclear leukocytes being later invaders. Ziegler[40] likewise emphasized the hemorrhagic character. Kundrat,[30] Sahli[41] and Birch-Hirchfeld[23] found the exudates very fibrinous and often hemorrhagic. Kuskow[2] found fibrin in varying amounts, generally present but seldom in large quantities. The exudate was often frankly hemorrhagic, usually catarrhal cells predominated, but sometimes the pneumonitis was frankly purulent. Leichtenstern[1] observed most frequently mixed catarrhal and fibrinous exudates. Finkler,[42] in whose cases streptococci were the most frequent invaders, found an acute interstitial pneumonia with catarrhal exudation in the alveolar septums and air sacs, and only a slight amount of fibrin. He compared the lesions with the changes seen in erysipelas.

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34. Fraenkel, A.: Deutsch. med. Wchnschr., p. 432, 1892.
35. Sokolowski: Schmidt's Jahrb. **228**:149, 1890.
36. Gaucher: Bull. Soc. méd. des hôp., 1890.
37. Frank, L.: Schmidt's Jahrb. **233**: 1890.
38. Simon, R.: Brit. M. J., 1892.
39. Pfeiffer, R.: Deutsch. med. Wchnschr., Nos. 2 u. 21, 1892; Ztschr. f. Hygiene **13**: 1893.
40. Ziegler: Quoted by Leichtenstern.
41. Sahli: Quoted by Leichtenstern.
42. Finkler, B.: Die Ak. Lungen entzündungen als Infections Krankheiten, Bonn, 1891. Also Deutsch. med. Wchnschr., No. 5, 1890.

During the present epidemic the pneumonitis was chiefly lobular. Symmers[11] found the exudate hemorrhagic, purulent and catarrhal with fibrin absent. Blanton and Irons[10] report the exudate fibrinous only once, and Opie[5] and his co-workers describe suppurative pneumonitis. Oberndorfer[27] found marked hemorrhagic infiltration, and, in the later stages, catarrhal and suppurative exudations. Chickering and Park[43] describe a staphylococcus pneumonia characterized by innumerable abscesses in the lung. Macallum[44] found the exudate to vary with the organisms present.

All the above indicates that according to time and place the disease changes have varied considerably.

TABLE 5.—Extent of Lung Involvement in Relation to Duration of Disease

Number of Lobes Involved	Duration of Disease			Total
	1 to 10 Days	11 to 20 Days	20 Days	
1	2 cases	4 cases	3 cases	9 cases
2	7 cases	3 cases	7 cases	17 cases
3	7 cases	8 cases	4 cases	19 cases
4	15 cases	19 cases	3 cases	37 cases
5	26 cases	11 cases	5 cases	42 cases

TABLE 6.—Distribution and Character of Bronchopneumonia

	Left Lung	Right Lung
Patchy Bronchopneumonia:		
Upper lobe	47	45
Middle lobe	..	38
Lower lobe	46	43
Confluent Bronchopneumonia:		
Upper lobe	35	37
Middle lobe	..	28
Lower lobe	55	56

The duration of the pneumonitis was estimated from the day that lung involvement was first observed to day of death (Table 4). Such an estimation is only accurate in a relative way, but certain interesting features were brought out thereby. It shows that eight of the 109 cases developed pneumonia within the first five days of the disease, and forty-three more within the first ten days, so that about half of the entire series presented lung involvement relatively early in the attack. The other half showed definite pneumonitis considerably later, fifteen cases developing it after the disease had persisted for twenty

43. Chickering, H. T., and Park, James H.: Staphylococcus aureus Pneumonia, J. A. M. A. **72**:617 (March 1) 1919.

44. MacCallum, W. G.: Pathology of Influenza Following Pneumonia, J. A. M. A. **72**:720 (March 8) 1919.

days. Once the pneumonitis was established it proved fatal within a relatively short time. Thus, in forty-five instances, the duration was 3.68 days, in thirty-seven it was 8.02 days, while in only three cases did the pneumonic process persist over twenty days, giving an average of twenty-six days. Further details are shown in the table. Pneumonitis occurred in 124 instances, in two cases none was present. In both of these a rapidly fatal epidemic meningitis occurred.

TABLE 7.—WEIGHTS AND MEASUREMENTS OF PRINCIPAL ORGANS
Average age: 25.21 years. Average weight: 76 kg. Average height: 174.8 cm.

Organ	No. of Cases	Range of Weights in Gm.	No.	Per Cent. of No. Examined	Average Weight in Gm.	Average Size in Cm.		
						Length	Width	Thickness
Brain	46	Below 1,400	18	39.1	1,300			
		1,400 – 1,600	22	50.0	1,452			
		Over 1,600	5	10.9	1,739			
Heart	66	Below 299	20	30.3	267			
		300 – 350	39	59.1	364.3			
		Over 400	7	10.6	429.3			
Left lung	65	Below 500	10	15.3	392.5			
		500 – 999	44	67.7	717.1			
		Over 1,000	11	16.9	1,328.6			
Right lung	64	Below 500	6	9.4	392.5			
		500 – 999	35	54.7	761.12			
		Over 1,000	23	35.9	1,343			
Spleen	68	Below 150	10	14.7	127.2	12.0	7.6	2.9
		150 – 249	31	45.6	192.9	13.6	8.4	3.5
		250 – 449	25	36.8	321	15.5	9.7	4.1
		Over 450	2	2.9	590	18.7	12.0	5.0
Left kidney	50	Below 150	5	10.0	135.4	11.1	6.0	3.25
		150 – 299	43	86.0	202.75	12.5	8.08	3.3
		Over 300	2	4.0	310	13.0	6.5	5.5
Right kidney	50	Below 150	5	10.0	135.8	11.0	5.9	3.2
		150 – 299	44	88.0	207.7	12.15	5.8	3.72
		Over 300	1	2.0	310	13.0	6.5	6.0
Liver	61	Below 1,500	4	6.6	1,248.75	25.5	18.5	7.9
		1,500 – 1,999	29	47.5	1,829.3	28.3	20.17	7.8
		Over 2,000	28	45.9	2,254.5	29.25	21.2	8.28

The amount of lung involvement in relation to duration of disease is shown in Table 5. This table shows that usually the involvement was extensive, since in 98 cases three or more lobes presented areas of consolidation. Both lungs were involved in 116 cases, the right lung alone in three, the left alone in five instances.

The weights of the lungs were estimated in sixty-five instances, details of which are shown in Table 7. In only a small per cent. relatively was the weight of either lung below 500 grams. In 67 per cent. of the cases the left lung averaged 717 grams; in 55 per cent. the right lung averaged 761 grams, in 17 per cent. the left lung averaged 1,328 grams, and in 36 per cent. the right lung averaged 1,343 grams. The lungs are, therefore, considerably heavier than in the average case

of bronchopneumonia, especially that of the aged. LeCount,[20] comparing the lung weight of influenzal pneumonia with that of croupous pneumonia, found the ratio of lung weight to body weight similar in these diseases. The anterior edges of the lungs were generally inflated, the compensatory emphysema being often very marked. Only in a relatively small number of instances were air bladders or distended, pearl-like, ruptured air vesicles seen. The posterior borders were usually the site of involvement, and had a slatey blue to reddish purple color. The upper lobes were almost as frequently attacked as the basal lobes, which seems one of the characteristics of influenzal pneumonitis. The consolidated areas varied considerably in size, frequently involving the greater part of entire lobes. True croupous lobar pneumonia, of the type commonly met with, was relatively rare, occurring only in thirteen instances. In seven of these it formed the only type of pulmonary consolidation, in the six others it was associated with bronchopneumonia.

The incidence of lobar pneumonia in association with influenza epidemics appears to have varied a great deal in different places and times, due probably to coexistence of two separate and distinct infections. Thus, during the Vienna epidemic of 1890, Kundrat[30] found it in one-half of his cases, and others have reported even higher figures. The probable explanation of this high frequency is that during the influenza period there coexisted an epidemic of lobar pneumonia. Opie[8] and his co-workers found thirty-six cases of lobar pneumonia in seventy-nine necropsies. Hall, Stone and Simpson,[29] in thirteen necropsies, found typical lobar pneumonia in eleven cases, and confirmed the diagnosis microscopically. Blanton and Irons,[10] in 123 necropsies, saw it only once. Nuzum,[21] Symmers[11] and others encountered only lobular pneumonia. The condition may be dismissed here with the statement that it presented no unusual feature, and we shall confine ouselves to a description of the influenzal pneumonitis.

The cut surface of the lung was generally very moist and excessively bloody, especially in the cases dying after a relatively short duration of disease. From the inflated anterior edges large amounts of lightly and heavily blood tinged, frothy serum could be expressed. In the posterior two-thirds larger and smaller areas of consolidation were present. These varied in color, size and consistency, resulting in a number of distinct pictures, often within the same lobe. Generally, the consolidated areas were indistinctly outlined and gradually faded into the surrounding hyperemic lung tissue. A marked tendency to become confluent was noted, and pseudolobar involvement occurred very commonly.

The texture was as diverse as the other features; smooth and velvety consolidations bordering on coarsely and finely granular neighboring areas. These granular consolidations resembled in every way the cut surface of a croupous pneumonia, except for their lobular character. The consistency ranged from definite necrotic softening to total firmness, and the color varied through all shades of red and gray. Only exceptionally were the consolidated areas definitely peribronchial. Now and then the interlobar septa were thickened and indurated areas were present. Atelectasis, due to obstruction of bronchial branches, was common, sometimes involving considerable areas. In a general way, the consolidations, according to their extent, might be classified as patchy and confluent or pseudolobar. Table 6 shows that there was but slight difference in the distribution of these two types in the various lobes of the lung; that the upper lobes were somewhat less confluent than the lower lobes, and that the middle lobes were the least affected.

Microscopically, as wide a variation was seen as in the gross appearance. The exudates had, however, sufficiently distinctive character to allow the division into three main groups. In the first, the exudate was chiefly catarrhal, consisting of large, desquamated, epithelial cells. In the second group the same features obtained, with the addition of a heavy fibrin network. In the third group, the exudate was mainly purulent, with the addition of fibrin. All three types often existed in the same lung. Commonly, even the same microscopic section presented all three of them, so that we might, as one of the main characteristic features of influenzal pneumonitis, take the great variation of the exudate. (Figures 13, 14 and 15 were purposely made from the same microscopic section. The various processes were distinct, but almost adjacent to one another.) This is readily explained if we remember that one or more organisms invade these tissues, and that each class of bacteria may set up distinctive inflammatory processes in adjoining or closely placed together alveoli. In addition to the cellular character of the exudates, there was usually a heavy admixture of red blood cells with large amounts of precipitated serum. It is very difficult to estimate the incidence of the three groups of exudates, since they so commonly occur together. By taking several sections from each lung and noting the predominant character of the exudate, the following grouping might be made:

Catarrhal bronchopneumonia..... 34 per cent.
Fibrinocatarrhal bronchopneumonia ..... 39 per cent.
Fibrinopurulent bronchopneumonia..... 27 per cent.

Such grouping, however, is only highly approximate and represents but the predominating character of the exudate in the majority of the sections examined. Fibrin, in varying amounts, could practically always be found in some sections, and in over two-thirds of the cases it was prominent. The exudates of the more catarrhal types generally presented pronounced swelling of the lining epithelium (Fig. 12), and not infrequently groups of alveoli were lined with huge cuboidal cells, giving the appearance of tubules and resembling the condition of the fetal lung. Such changes, as is well known, are often seen after indu-

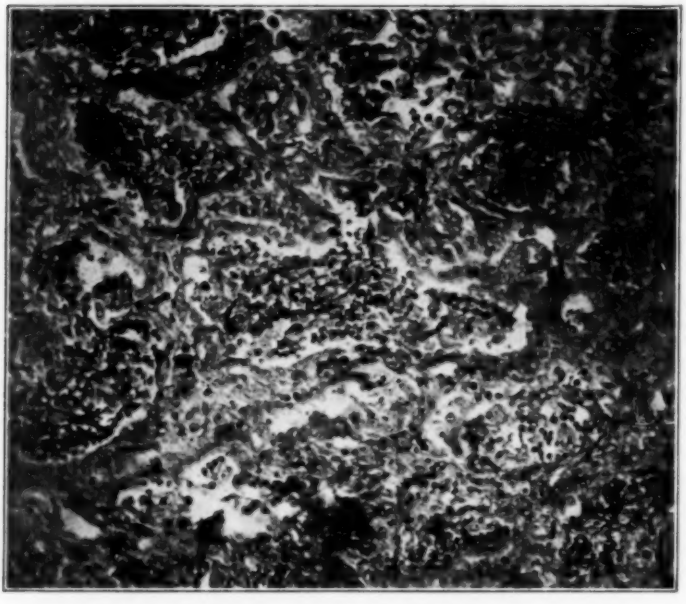

Fig. 12.—(Lung.) Hyperplasia (anaplasia?) of pulmonary epithelium. Note the uniform hyperplasia of the epithelial lining. This photograph does not represent the most pronounced proliferation, but the average.

rative bronchopneumonic processes, but only rarely is this extreme proliferation encountered in an acute pneumonitis. In some sections the condition was so uniform as to make one consider the possibility of a reversion to fetal types, an anaplasia produced by excessive stimulation of the lung epithelium. It is doubtful whether such anaplastic changes ever occur in acute inflammations, and our statement here is merely an analogy.

In sections where definite fibrosis was present—usually in cases where the pulmonary infection had persisted for a relatively consid-

erable time—such proliferation of the lining membrane was likewise frequently encountered. Occasionally the alveolar membrane was intact, but more generally a part, at least, was desquamated, and these huge cells were lying free in the air sacs (Fig. 13).

All stages of cellular degeneration could be observed, the most noteworthy being vacuolization with shrinkage of the nucleus. Phagocytosis was often seen; the phagocytized structures being most often red blood cells, polymorphonuclear leukocytes and cellular debris. Bacterial phagocytosis was relatively infrequent in the large cells, but

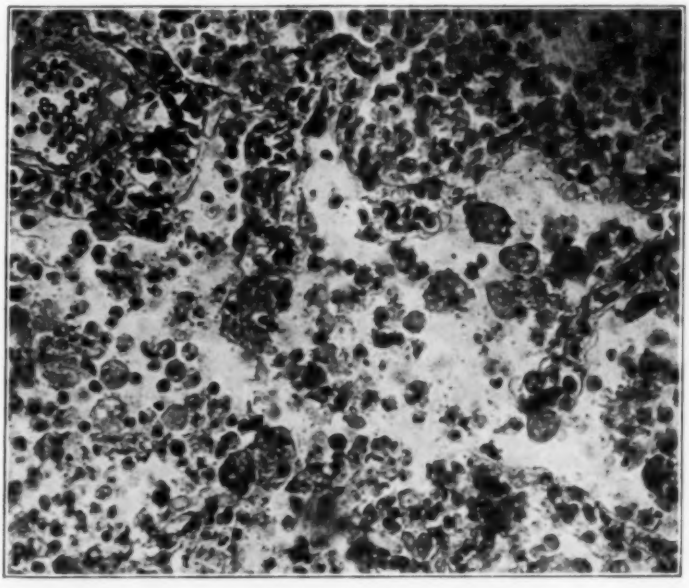

Fig. 13.—(Lung.) Catarrhal bronchopneumonia. Note presence of huge, often vacuolated, desquamated epithelial cells. Fibrin is absent. The alveolar capillaries are markedly distended.

quite common in polymorphonuclear leukocytes. Sometimes the epithelial cells were fused together, forming huge, syncytial masses, apparently consisting of from three to five fused cells and measuring up to 60 microns in diameter. These giant structures frequently contained inclusions of red cells and leukocytes, and are probably degenerative in character. Besides the lining cells the exudate consisted chiefly of precipitated serum and red corpuscles, polymorphonuclear elements being uncommon. Definite hemorrhages were frequent and often involved large areas. The alveolar capillaries were hugely dis-

tended and often contained hyaline conglutination thrombi. Generally, the walls were well preserved and cellular infiltration was rare. The perivascular and peribronchial spaces contained cells of the same type as those described.

This catarrhal type of pneumonitis predominated early in the epidemic and throughout the epidemic in patients dying after a relatively short illness, and we believe that the changes enumerated are more directly due to the virus of influenza than to the associated bacteria. In fact, we are convinced that the pronounced epithelial proliferation and the marked hyperemia constitute the essential early lesions of true influenza.

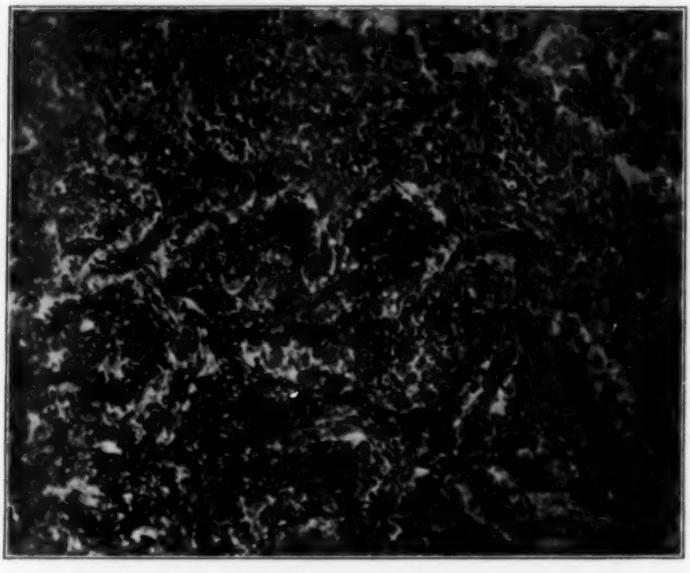

Fig. 14. — (Lung.) Fibrinocellular bronchopneumonia. Note network of fibrin and presence of large epithelial cells. This was the most common picture seen in influenzal bronchopneumonia.

The second type of pneumonitis was fibrinocatarrhal in character, and differed from the preceding not only in the addition of large amounts of fibrin, but in cellular reaction. Catarrhal cells were still present in relatively large numbers and presented the general characters mentioned above, excepting that more intense degenerative changes were seen. The fibrin occurred in the form of dense networks, consisting sometimes of fine, sometimes coarse, strands (Fig. 14), and it was generally more pronounced at the periphery of the air cells.

Polymorphonuclear cells were present in greater numbers than in the preceding forms. Red blood cells were abundant, but generally not so excessive as in the preceding type. The alveolar walls were frequently ruptured and infiltrated with mononuclear and polymorphonuclear leukocytes, and often showed a fibrin network. We look on this type as an intermediate stage in the disease process.

The third group was fibrinopurulent or purulent in character, the exudate containing relatively few epithelial cells, while polymorphonuclear leukocytes were abundant (Fig. 15). Fibrin was present in varying amounts. The alveolar contents were rarely hemorrhagic,

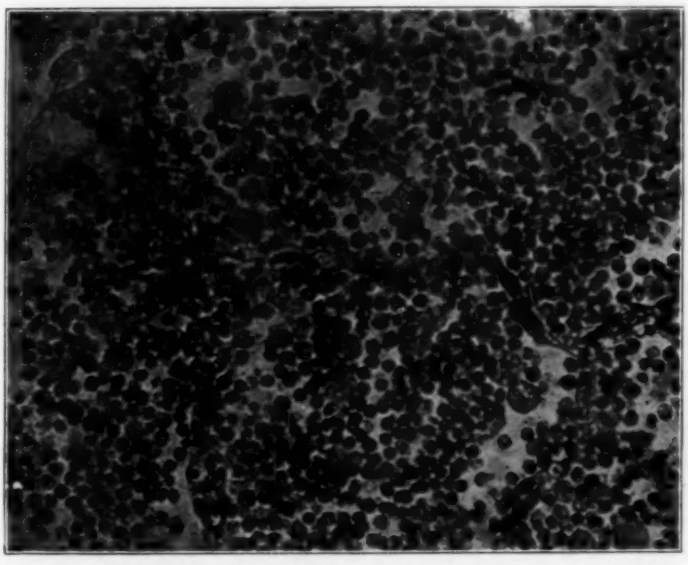

Fig. 15.—(Lung.) Suppurative bronchopneumonia. The cellular exudate consists chiefly of polymorphonuclear cells, with here and there a few large degenerated epithelial cells.

though sometimes a few red cells were seen. Serum was seldom as pronounced as in the earlier stages. Typical plasma cells were frequently observed in considerable numbers in the exudate as well as in the lymphatics and alveolar walls. These last often showed widespread destruction, and large areas of necrosis were often seen (Figs. 16 and 17).

Fibrosis was not infrequent. The bronchial walls were often entirely destroyed and abscesses were many times encountered. We consider this the end stage of influenzal pneumonitis. It occurred at

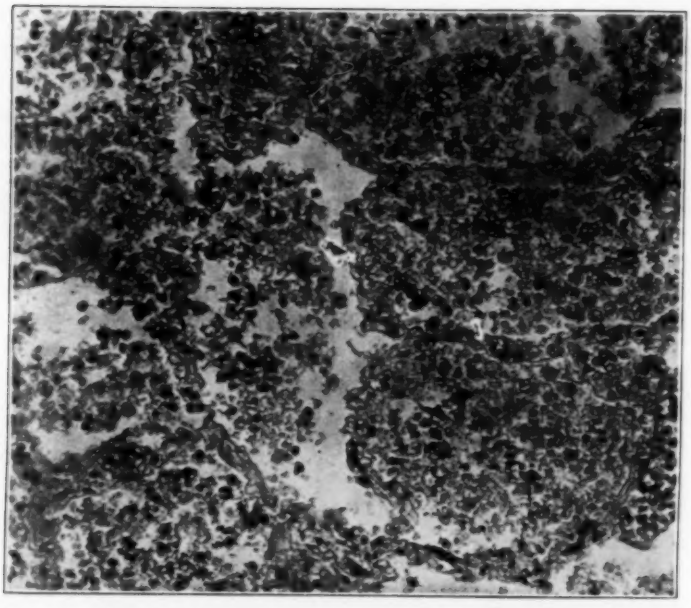

Fig. 16.—(Lung.) Suppurative pneumonia with partial destruction of the alveolar wall. The exudate here is older than in the preceding figure, and the various cells are considerably more degenerated.

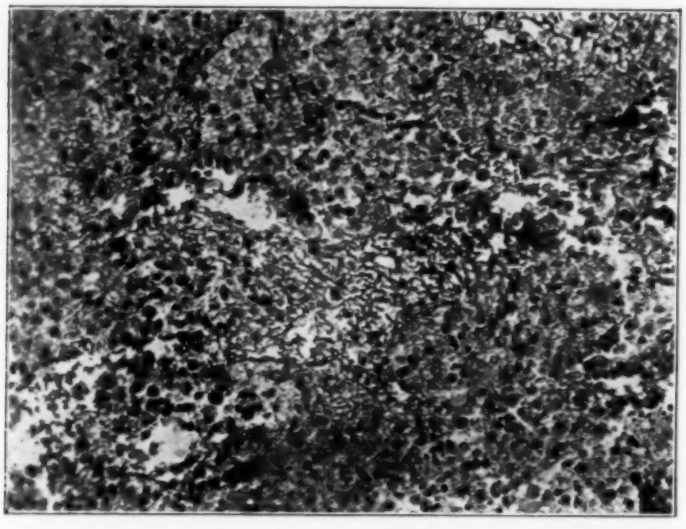

Fig. 17.—(Lung.) Suppurative bronchopneumonia with areas of necrosis. The alveolar walls here are entirely destroyed and necrotic areas are everywhere seen. This is a later stage than that shown in the preceding figure.

a later period in the epidemic when the duration of the illness was considerably longer than in the earlier part of the epidemic, and when the pneumonic processes had persisted for some time. It is the second and third type of influenzal pneumonitis which is probably produced by the commensals of the virus of influenza.

TYPES OF INFLUENZAL PNEUMONIA ACCORDING TO THE ORGANISMS PRESENT

An attempt was made to correlate the anatomic findings with the bacteriologic results, and to classify the types of pneumonitis encountered according to the bacteria present. As will be seen in the bacteriologic part of this paper, the micro-organisms which were most often isolated were: *B. influenzae,* hemolytic and nonhemolytic streptococci, pneumococcus of various types, *M. catarrhalis* and staphylococcus. These were usually present in various combinations. Indeed, it was not uncommon to find most or all of them in cultures from the different lobes of the same lung. It was, therefore, exceedingly difficult to attribute this or that anatomic change to any special bacterial type. The fact that all of these bacteria must be looked on as commensals, or as secondary or tertiary invaders of the pathologic tissue prepared by the virus of influenza, make separation on an etiologic basis generally quite impossible. MacCallum,[44] who classified his cases, apparently had less of a mixture of bacteria than were present in our series, and he was able to separate the types of pneumonitis caused by the pneumococcus, streptococcus and the influenza bacillus.

It was the custom here to take cultures from all lobes of the lungs, as well as from the principal organs. In only two instances were pure cultures of the influenza bacillus isolated; once the staphylococcus, once *M. catarrhalis,* five times the nonhemolytic streptococcus and somewhat more frequently the pneumococcus and hemolytic streptococcus were found in an unmixed form in the lungs and elsewhere. If we add to this the difficulty in isolating this or that bacterium we introduce an added source of error; nevertheless in the patients where pure cultures of one type were obtained, a correlative study was undertaken.

We have already stated that it was not uncommon to find several distinct types of exudates within the same lung, and even within the same microscopic section, and it was not surprising, therefore, to obtain the same results when comparison of the anatomic and bacteriologic studies was undertaken. Thus, for instance, in the two cases where *B. influenzae* occurred in pure culture, the exudate was fibrinocatarrhal in the majority of sections of one case, and purulent, with relatively small amount of fibrin, in the other. The same condition

was present in the staphylococcus and *M. catarrhalis* cases, while in the pneumococcus and hemolytic and nonhemolytic streptococcus cases, the results were even more confusing. Thus, in nineteen cases where the hemolytic streptococcus predominated, the lung exudate in the majority of the sections was catarrhal eight times, fibrinocatarrhal five times, fibrinopurulent four times, purulent with areas of necrosis twice. The nonhemolytic streptococcus and the pneumococcus cases showed a similar discrepancy. It seems, therefore, it is not feasible to divide the pneumonitis of influenza on bacteriologic basis excepting in a general way, and this we can do by considering the mixtures of bacteria that predominated at the various stages of the epidemic and in the different periods of the disease, remembering always that we deal with a definite morbid process, more or less modified by commensual or invading organisms.

In this general way we feel that the first picture of influenzal pneumonitis, chiefly catarrhal in type, was produced mainly by the *B. influenzae* and the nonhemolytic streptococcus (Figs. 12 and 13). The second form of pneumonitis, fibrinocatarrhal, was probably the result of pneumococcic and nonhemolytic streptococcic activity (Fig. 14), while the last form, fibrinopurulent or purulent in character (Figs. 15, 16 and 17) had the staphylococcus, *M. catarrhalis* and hemolytic streptococcus as the chief invasive factors. Further than this we do not feel justified in going, and it seems to us that in the multiformity of lung changes present lies the chief characteristic of influenzal pneumonitis. In other places, where fewer micro-organisms are endemically or epidemically present, a separation into distinct types is, of course, possible, and should rightly be undertaken. The diversity of the pathologic and bacteriologic picture in this and preceding epidemics speaks for the pleomorphic character of the disease.

Spleen.—The statements in the literature concerning the size of the spleen vary greatly, and this Kuskow,[9] who seems to have studied the subject most thoroughly, explains as depending on the severity of the epidemic or on individual cases. According to him, during the epidemic of 1889-1890 in France the spleen was increased to twice its size and more. In Switzerland, Finland and Russia the majority of the authors found the spleen rarely enlarged, and sometimes decreased. In his own forty cases (Russia) the spleen was actually smaller, and very markedly decreased in size in twenty-eight. In the present American pandemic slight enlargement seems to have been the rule, with relatively few acute splenic tumors (Blanton and Irons,[10] Symmers[11]). The details of our findings were calculated for sixty-eight cases (Table 7). In ten of these cases the spleen weighed less than 150 grams, in thirty-one it weighed between 150 and 249 grams, with

an average of 195 grams. In twenty-five it weighed between 250 grams and 449 grams, with an average of 321 grams. In two cases it weighed more than 450 grams, with an average of 590 grams. Further data as to weight and measurements are given in the table. It would seem then, that in more than 80 per cent. of the cases the spleens were definitely enlarged, and in almost one-third of the total number they were considerably increased in size. Definite diminution never occurred, the spleen in no instance weighing less than 100 grams.

The capsule was generally tense, the external color reddish brown to purplish red, consistency slightly flaccid, occasionally much softened. The cut surface was usually uneven, moist and often very bloody. The

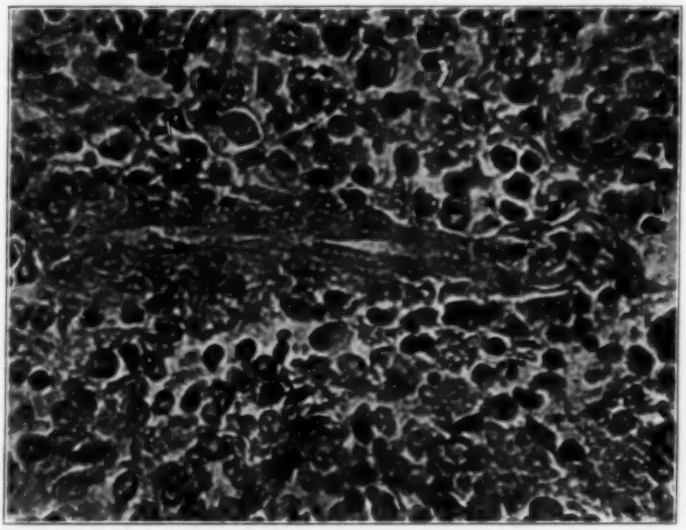

Fig. 18.—(Spleen.) Note swelling of arterial lining. The vascular lumen is almost occluded.

trabeculae could only rarely be recognized distinctly. The follicles were plainly visible or somewhat prominent in fifty-seven instances, and indistinct or entirely obscured in sixty-nine instances. The pulp was usually softened, and in about 20 per cent. of the cases it was definitely mushy. The duration of the disease process, the period of the epidemic, the size of the spleen and its follicular or diffuse character did not appear to exhibit any constant relation. Microscopically, the commonest change consisted in the excessive blood contents; often large areas were flooded with red cells, constituting undoubted hemorrhages, many of these cells being shadow rings. An endothelial hyper-

plasia of the vessels and sinuses was usually present and often pronounced (Fig. 18). Oftentimes desquamated endothelial cells were found free in the venules and arterioles, occasionally obstructing their lumen; hyalin and conglutination thrombi were likewise present. Widespread necrosis of the reticulum commonly occurred, partly due, probably, to the hemorrhages and partly to toxic action. Now and then the arterial walls presented a smooth, homogeneous staining, evidencing toxic hyaline degeneration. Elsewhere definite hyperplasia was present, manifesting itself by greatly increased numbers of large mononuclear splenic cells. Polymorphonuclear cells were rarely met with, and then only in small numbers. The malpighian bodies were

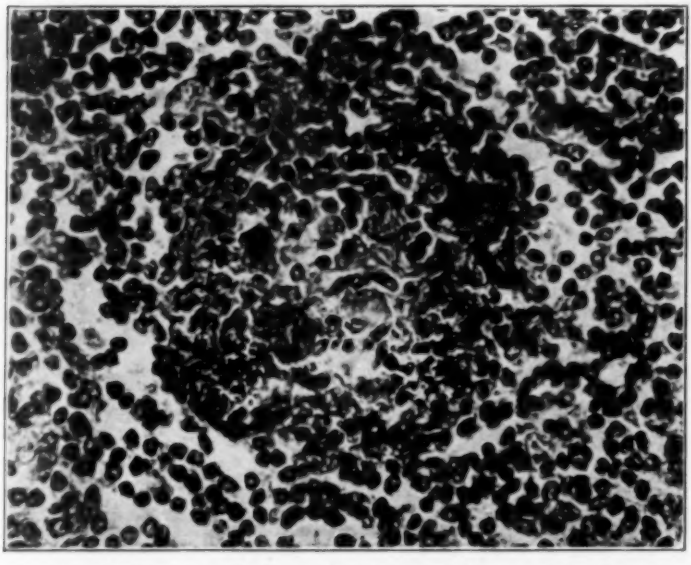

Fig. 19.—(Spleen.) Beginning hyalin degeneration of germinal centers of follicles. Note the huge, even-staining cells in center of photograph. This is the early stage of the process shown in Figure 20.

generally loosely arranged, with many large, pale staining, germinal lymphocytes. Within the follicles one frequently encountered eosin staining, smooth, hyaline areas, occasionally of considerable size. On minute inspection these areas seem to be composed of huge partly fused, indefinite staining, degenerating cells (Figs. 19 and 20). Similar necrotic areas have been found in diphtheria, scarlet fever and other acute infections (McCallum[45]).

45. McCallum, W. G.: Textbook of Pathology, Philadelphia, W. B. Saunders Co., 1916.

Fig. 20.—(Spleen.) Toxic hyaline degeneration of germinal centers of splenic follicles. This represents a later stage of the preceding figure. Note that the entire germinal center consists of fused degenerated cells; a few of the nuclei are still present.

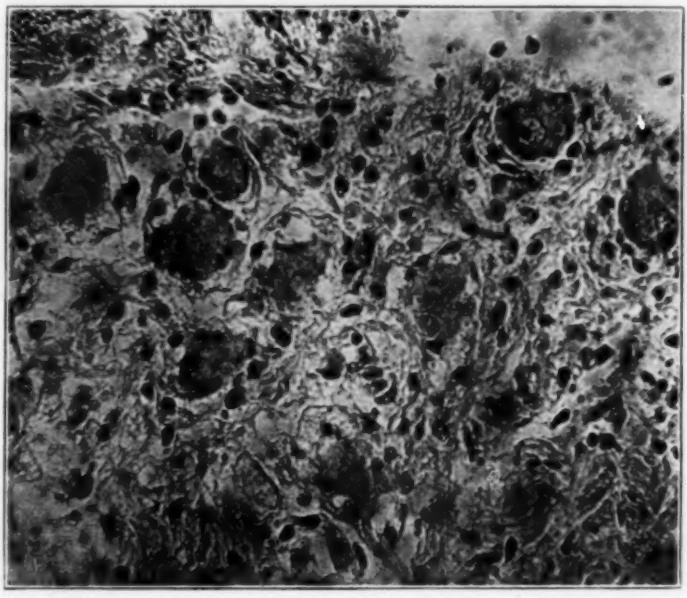

Fig. 21.—(Semilunar ganglion.) Acute cloudy swelling and degeneration of ganglionic cells. All stages, from simple cloudy swelling to almost total disappearance of the cells, are shown. Note the nuclear changes varying from eccentric position (middle of photograph) to total chromato-lysis (left side of photograph). Compare the cellular changes with a nearly normal cell shown in the upper right corner of the photograph.

Semilunar Ganglia.—These structures in practically every instance were slightly swollen and occasionally of a faint pink color. There was no appreciable change in the consistency. The cut surface was usually moist, often decidedly pinkish, and a number of bleeding points were always seen. Microscopically (Fig. 21), the ganglion cells were swollen, devoid of definite outline, with a granular cytoplasm which stained poorly and did not show Nissl granules. The nuclear changes varied from loss of nuclear outline to poor or excessive staining, granularity, and often total disappearance of the nucleus. The nucleoli, as a rule, remained, but occasionally they likewise disappeared. Extreme changes consisted in loss of the entire cell. The above enumerated

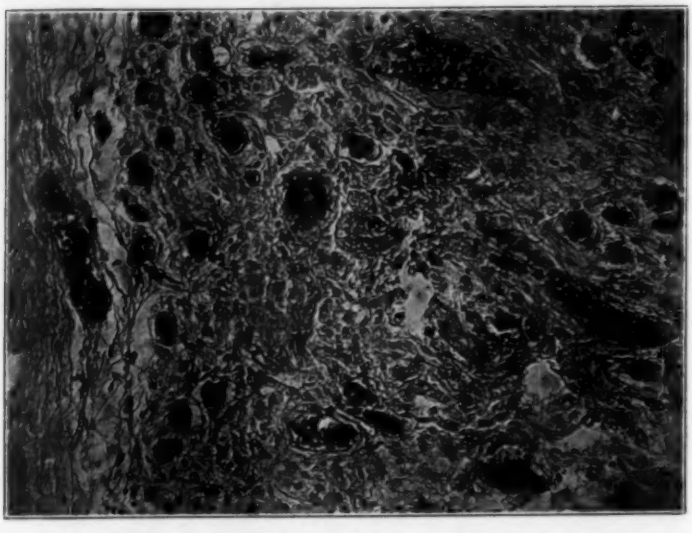

Fig. 22.—(Semilunar ganglion.) Marked congestion and degeneration of ganglion cells. The cellular changes are similar to those pictured in the preceding photograph. Note dense congestion of vessels.

alterations usually affected only isolated cells or groups of cells, for in other parts of the section the structures were normal. The condition was comparable to the ganglionic changes in the cerebral cortex and seems to point to the widespread toxic effects of the virus. The vascular changes were similar to those described in other organs, such as definite hemorrhages and practically always, marked congestions (Fig. 22). Occasionally, the perivascular lymphatics were dilated and packed with large and small round cells. The interstitial substance was often loosely arranged.

Suprarenals.—In three instances frank hemorrhages in the suprarenal substance, enlarging the organ to about twice its normal size, were present. In twenty cases the suprarenals showed no gross changes. In the remaining 103 cases there was slight increase in size and definite congestion. In these latter cases the outside color was pinkish brown, and the cut surface decidedly bloody. The outer zone of the cortex was generally narrow and pale grayish yellow, rarely presenting the deep orange yellow tint so frequently seen in the suprarenal cortex. The intermediate zone was a deep reddish brown and exuded blood, while the medulla varied from a reddish gray to a deep red. Microscopically, extreme congestion and frequent small hemor-

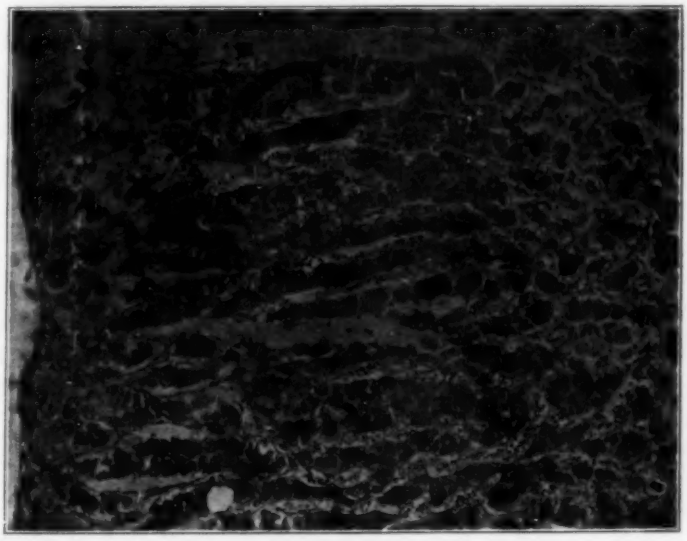

Fig. 23.—(Suprarenal.) Lipoid exhaustion. Note absence of lipoid granules, moderate edema, and, in places, cellular swelling and loss of outline.

rhages were found, usually involving the medulla and intermediate zone. The cells of the cortex appeared slightly swollen and usually devoid of their lipoid granules. This lipoid exhaustion was observed almost constantly (Fig. 23). Other cells appeared in the state of acute cloudy swelling, with indefinite cell outlines and poorly staining nucleus. The interstitial substance was usually arranged loosely and was definitely edematous. Focal necrosis, with small round cell infiltrations, was occasionally observed. In a number of the gland cells, especially of the cortex, numerous deep blue staining, coarse granules were encountered. We shall refer to this in the discussion of the liver, where

similar granules were often observed. Very occasionally diffuse infiltration with polymorphonuclear cells, pointing to an acute inflammatory suprarenalitis, was seen.

Genito-Urinary Tract. — Kidneys: The details of the weights and measurements were tabulated for fifty pairs of kidneys, and are given in Table 7. In 10 per cent. both kidneys weighed less than 150 gm. each. In eighty-six, or 88 per cent., the weight of each organ averaged 202 and 207 gm., respectively. In four, or 2 per cent., respectively, each organ weighed 210 gm. Both kidneys were of the same weight in 7 per cent., the left was heavier than the right in 54 per cent. and the right kidney heavier than the left in 39 per cent. of the cases.

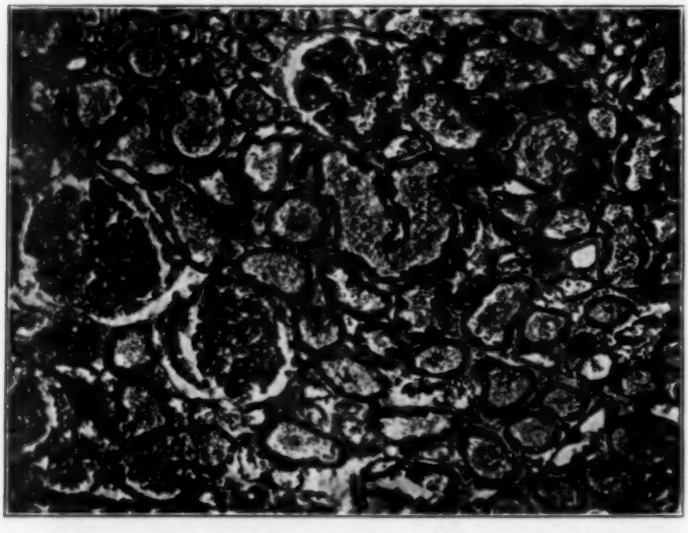

Fig. 24.—(Kidney.) Acute parenchymatous degeneration. Note presence within tubules and capsular spaces of granular precipitate. The epithelial lining is frequently degenerated and often necrotic. The capsular epithelium is somewhat precipitated.

The measurements corresponded to the size and are given in the table. This means that in 90 per cent. of the examinations the kidneys were somewhat increased in size or weight. In every instance parenchymatous changes, usually of mild degree, but often quite severe, were observed. It was not possible, grossly, and frequently impossible minutely, to decide whether the condition present should be looked on as an early parenchymatous nephritis, or as a transitory cloudy swelling. Definite nephritis was present in about 10 per cent. of the cases, but generally the organs were flaccid, with an easily stripping

capsule, leaving a smooth, grayish red, often mottled, surface, on which the stellate veins often stood out prominently. The cut surface was, as a rule, moist and bloody. The cortex was usually moderately increased in width, the cut edges gaping slightly, and, in a number of cases, considerably. The glomerular markings were sometimes washed out, but at other times very definite, and, in a considerable number of instances, the glomeruli and cortical striations were prominent. The corticomedullary junction was, as a rule, very indefinite. The medullary junction was usually very indefinite. The medullary striations varied, but, as a rule, were distinct. The pelvic mucosa usually presented injection, and, in about 30 per cent. of the cases submucous, petechial hemorrhages were encountered.

Microscopically, the kidney picture was quite uniform, varying only in degree (Fig. 24). The interstitial substance was moderately edematous, the glomeruli where large, the capsule of Bowman was not thickened. The capsular epithelium was swollen and proliferated in about 20 per cent. of the cases. Multiple layers of capsular epithelium were met with in a few instances. The capsular space, in 50 per cent. of the cases, contained a granular, eosin staining precipitate. The tufts were large because of vascular cŏngestion. The endothelium was swollen with large nuclei, but there was no evident active multiplication. Frequently, hyaline and conglutination thrombi were seen. The tubular epithelium was generally swollen, the cell outlines poor, the cell borders ragged and the lumen filled with granular debris. Often vacuolization was observed. The nuclear changes ranged from poor staining reactions to total absence. In one instance, a large part of the kidney appeared necrotic. Small microbic abscesses were present in only one instance (Fig. 25). In every case the convoluted tubules were more affected than the straight tubules. The degeneration and necrosis of the epithelium was rarely uniformly distributed, sometimes entire tubules, or groups of tubules, were attacked, with apparently normal epithelium in close proximity. It would seem from the literature that acute nephritis appears less frequently than in most infectious diseases. During the epidemic of 1889 and the succeeding years the changes found closely resembled those seen here. Thus, Wallis,[24] Ribbert,[22] Weichselbaum,[25] Kuskow,[2] and others reported cloudy swelling, with occasional glomerular nephritis. Hemorrhagic nephritis appeared uncommon.

Total necrosis of an entire kidney was described by Beneke[46] and once by Kuskow.[2] The former compared this to the necrosis resulting from ligation of the renal vessels and believed it to be due to vascular spasms. No explanation can be offered as to the necrosis in our case,

46. Beneke: Schmidt's Jahrb. **226**: p. 111.

but it was probably toxic rather than infectious. Stone and Swift,[18] in fifty-five necropsies, found acute parenchymatous nephritis twenty-three times and cloudy swelling twenty times (gross diagnosis). Dever, Boles and Case,[47] in two necropsies, found well marked parenchymatous nephritis. Nuzum[21] and his co-workers report the kidneys heavier than normal and the seat of a parenchymatous degeneration. Blanton and Irons,[10] in 123 necropsies, found acute nephritis in three and cloudy swelling of the kidneys in twenty-one cases. Symmers,[11] in twenty necropsies, observed changes comparable to those seen here. The kidney changes observed here and elsewhere during the epidemic seem to be of the nature of a parenchymatous degeneration, with edema, rather than of a productive nephritis, although this too has occurred several times.

Fig. 25.—(Kidney.) Bacterial embolism and abscess. Note darkly stained bacterial mass and surrounding necrosis and cellular infiltration.

Ureter, Bladder and Prostate.—The ureter, in its upper fourth, frequently showed submucous, hemorrhagic extravasations, similar to those observed in the renal pelvis. The rest of the mucosa was occasionally moderately injected. The urinary bladder was similarly affected, showing injection, and commonly submucous, petechial hemorrhages.

47. Dever, Francis J., Boles, Russell S., and Case, Eugene A.: Influenza at the U. S. Naval Hospital, League Island, Va., J. A. M. A. **72**:265 (Jan. 25) 1919.

Prostate.—No gross nor microscopic changes were observed, with the exception of slight congestion. The prostatic acini presented no noteworthy alterations.

Seminal Vesicles, Spermatic Cords and Testicles.—The seminal vesicles were generally filled with a viscid, sometimes slightly turbid fluid. The spermatic cords presented no gross changes. The testicles very frequently possessed a moist, definitely bloody, cut surface and were of softened consistency. The cells, microscopically, were commonly swollen and ragged; cessation of spermatogenesis was frequently seen.

Gastro-Intestinal Tract.—Tongue: The tongue was often reddened, but no characteristic changes, as in typhoid or scarlet, were observed. The mucosa of the mouth and posterior pharynx was likewise often reddened. Microscopically, the lymphoid tissue was frequently very prominent. This same condition has been observed by Oberndorfer,[27] but the youthful age of our patients makes it unlikely that we are dealing with a pathologic change, although the lymph tissue generally in the body is proliferated above the normal state for the age of these patients.

Tonsils and Thyroid.—An acute tonsillitis was occasionally encountered, but it is probably coincidental. The thyroid was now and then somewhat enlarged, but presented no noteworthy microscopic changes.

Pharynx, Esophagus and Stomach.—The mucosa was frequently dusky. The lymph follicles, in the lower part of the esophagus, were usually prominent. In the stomach we found almost constantly extensive submucous, petechial, hemorrhagic extravasations, not confined to the dependent parts, and probably not postmortem in origin since they were found in bodies necropsied within an hour or so after death. The condition is comparable to the hemorrhagic extravasation noted beneath mucous and serous surfaces and in the skin. The stomach contents, which were generally fluid, often had a light brown or reddish brown tint, due, probably, to slight leaking of the extravasated areas. No other gross or microscopic changes occurred.

Liver.—The details of the weight and size of the liver were estimated in sixty-one instances. In 7 per cent. the liver weighed less than 1,500 gm; in 47 per cent. the weight averaged 1,829 gm.; in 46 per cent. the weight averaged 2,254 gm. Further details are shown in Table 7. In over 90 per cent. of the cases the liver was definitely increased in size and weight. Nuzum,[21] Lyon[6] and others found the liver likewise heavier than normal. The consistency was generally flaccid, occasionally definitely soft. The lower edge was, as a rule, rounded, the capsule smooth and translucent and the subcapsular lobu-

lation generally indefinite but sometimes prominent. The cut surface was generally slightly but frequently considerably bloody. The lobulation appeared washed out. The translucency of the tissue was, in the majority of instances, dull, gray and often parboiled. In about one-third of the cases the centers of the lobules were large and deeply congested. Frequently, especially near the periphery of the organ, pale, yellowish fatty areas were seen. In a number of cases lobulation appeared usually distinct, the centers being very large and dull brownish red or yellowish red, with a narrow, grayish brown peripheral zone. Very exceptionally the surface possessed a fatty sheen; evidences of biliary pigmentation were never observed grossly.

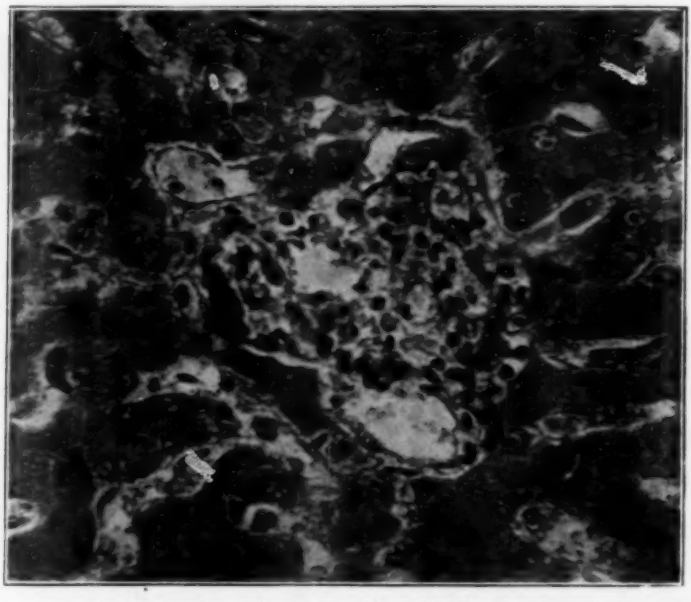

Fig. 26.—(Liver.) Small focal necrosis. The necrotic areas here involve only a small part of the liver lobule. A few round cells and some degenerating nuclei are present in the necrotic area.

Microscopically, the principal change was albuminous degeneration, the cells being large, with cloudy cytoplasm, the nucleus presenting various degenerative changes. Inconspicuous biliary pigmentation was common but not prominent. A few areas of fatty infiltration were frequently seen, but this was never excessive. Fatty degeneration was rare, but hydropic degeneration was common. In fully 50 per cent. of the cases areas of focal necrosis were present. In 11 per cent. these

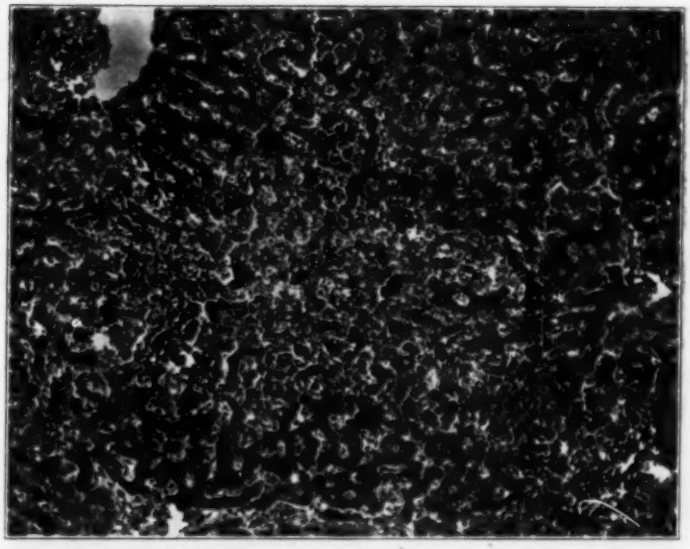

Fig. 27.—(Liver.) Acute toxic central necrosis. The necrotic area involves about two thirds of the liver lobule. The cells in this region show various stages of degeneration, ranging from multiple vacuolization (fatty degeneration) to entire disappearance of the cell. This condition may be looked upon as the preceding stage of acute yellow atrophy illustrated in Figure 28.

Fig. 28.—(Liver.) Acute toxic central necrosis. This illustrates a somewhat more advanced condition than shown in Figure 27.

were pronounced and large, and, in one instance, a marked acute, yellow atrophy was present. The focal necroses, in the majority of instances, were relatively small (Fig. 26), involving only groups of a few liver cells, but all degrees were present (Figs. 27 and 28) with an extreme condition in one case where practically no normal liver cells occurred (Fig. 29). The necrotic tissue consisted of structureless, eosin staining cells, intermingled with free nuclei, lymphocytic elements and moderate numbers of plasma cells with relatively few polynuclear elements. In the cases of acute yellow atrophy all but the periphery of the lobules was destroyed, the peripheral cells being swollen and

Fig. 29.—(Liver.) Acute yellow atrophy. Practically no normal liver tissue is present. Here and there multi-vacuolated and partly degenerated liver cells are shown near the periphery of the lobules. For the details see Figure 30.

multivaccuolated and presenting pronounced nuclear changes (Fig. 30). The Kupfer cells throughout the liver, but especially in the necrotic areas, possessed swollen, oval nuclei and large amounts of cytoplasm. Red cells were present in moderate numbers. The gross appearance of this liver gave little evidence of the excessive microscopic changes. It weighed 1,925 gm., was softened, of reddish brown color, the cut surface presenting very large, reddish brown lobular centers with a pale periphery. Kuskow[2] usually found albuminous degeneration, often focal necrosis, but never fatty degeneration.

Fig. 30.—(Liver.) Acute yellow atrophy. This photograph illustrates the condition of the cells at the periphery of the necrotic areas shown in Figure 29. Note the marked fatty degeneration and nuclear changes.

Fig. 31.—(Liver.) Bacterial phagocytosis and lysis by liver cells. Note dark granules in cytoplasm. These granules stain blue with basic dyes.

Frequently, the liver cells contained fine, blue-staining granules (Fig. 31). Searching with the oil immersion lens one occasionally saw small groups of micrococci in the sinusoids, and it seems that these granules were similar to those described by Adami[48] in his subinfection theory as being the final stages of bacterial destruction. The same doubtless holds true of the blue granules described in the adrenal. Sometimes this condition could be studied exceptionally well, especially when only small numbers of micro-organisms were present in the sinusoids, for here all stages of bacterial lysis could be observed in the adjoining liver cells. The periportal connective tissue was rarely

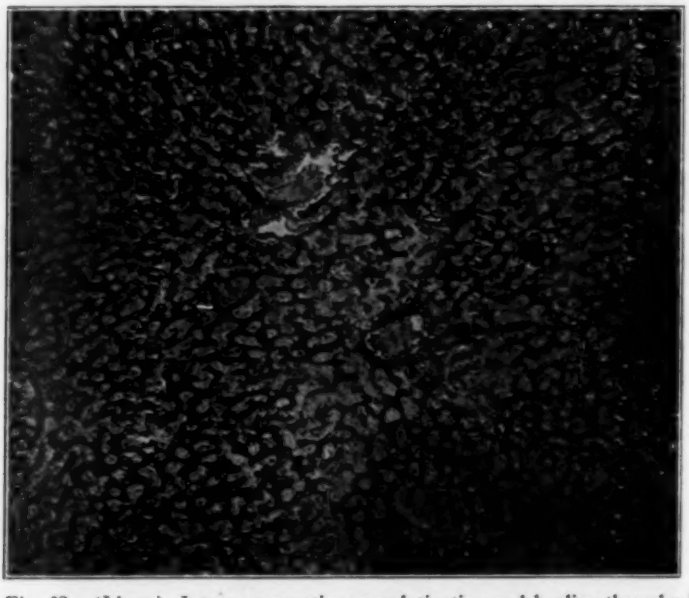

Fig. 32.—(Liver.) Intense congestion, conglutination and hyaline thrombosis. Note that the red cells in the sinusoids and venules have fused into a smooth hyaline mass.

proliferated, but occasionally a lymphocytic or leukocytic infiltration of unimportant degree was observed. The number of biliary ducts was never increased, but in extensive necrosis there was a swelling, without multiplication of the component cells. The vascular changes were similar to those described elsewhere, and frequently consisted of intense congestion and hyaline or conglutination thrombosis (Fig. 32).

48. Adami, J. George: Principles of Pathology, Philadelphia, Lea and Febiger **1**:425, 1909.

Pancreas.—The gross changes were slight and consisted in flaccidity and dusky gray appearance, and the cut surface was often moderately bloody. Microscopically, the vascular changes were of the usual type. The cells of the acini were frequently swollen, with poor staining or faulty staining nuclei. The ductal cells presented similar changes, and occasionally were desquamated. The most important alterations were noted in the islands (Fig. 33). These were indefinitely outlined; their cells had a washed out appearance, and were poorly differentiated from one another. They were increased in size, often fragmented, and usually presented pronounced nuclear changes

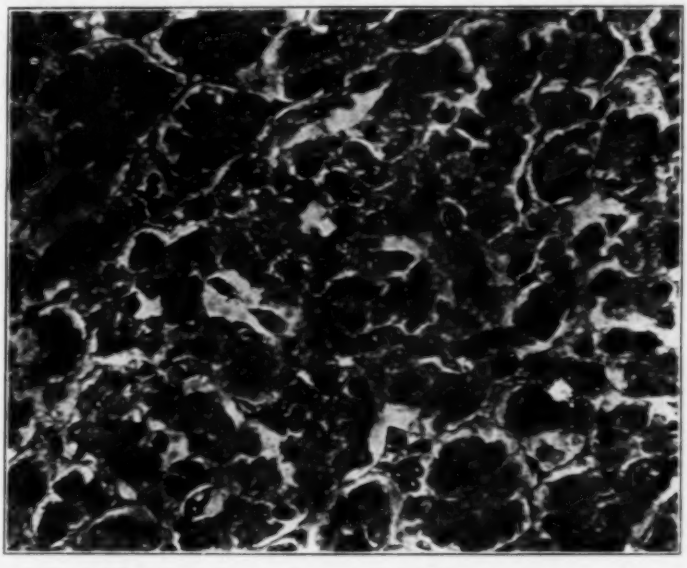

Fig. 33.—(Pancreas.) Toxic degeneration of islands of Langerhans. The islands are indistinctly outlined and consist of poorly differentiated, swollen and partly degenerated cells.

or absence of nucleus. This is a similar toxic degeneration to that observed in the liver, spleen and elsewhere.

Mesenteric Lymph Nodes.—The lymph nodes were moderately swollen, but never were larger than a bean. Their cut surface was slightly moist and had a grayish pink appearance. Frequently, they were definitely reddened. Microscopically, there was a slight sinus catarrh, slight lymphoid proliferation, and a moderate edema, the changes being comparable to those in the peribronchial lymph nodes, although always of a much less degree.

Intestines. — Practically always, larger or smaller areas of the mucosa were definitely congested and frequently submucous hemorrhages were seen (Fig. 34). The mucosa was commonly swollen, gray and turbid, and, in the duodenum, much bile stained. In the majority of instances, the lymphoid tissue was definitely hyperplastic; this condition being especially pronounced in the ileum. Of ninety-seven cases, where notes as to the lymphoid status were made, the solitary follicles and Peyer's patches were markedly hyperplastic in forty, the hyperplasia being slight, or not present, in the remaining fifty-seven instances. In the pronounced cases the follicles were swollen to the size of two or three millimeters, and usually surrounded by a definite

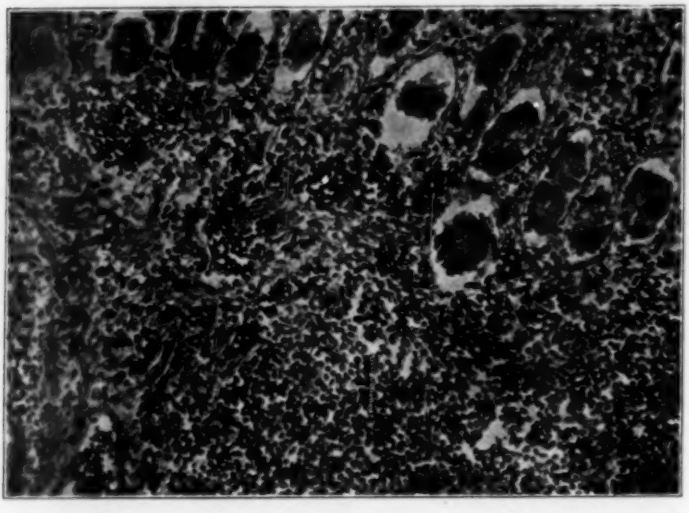

Fig. 34.—(Intestines.) Congestion and hemorrhage. Note intense congestion and areas of hemorrhage involving the mucosa and submucosa. The lymphoid tissue is proliferated.

hemorrhagic zone, giving the mucosa a coarsely granular appearance. The Peyer's patches were well raised above the surface and of a grayish brown color. Occasional central liquefaction necrosis of the follicles was encountered, resulting in the formation of vesicular structures with turbid contents. Microscopically, congestion and submucous hemorrhages were the rule. The lymphoid tissue was actively hyperplastic, presenting many large lymphoid cells and some endothelial elements. Kuskow[2] has observed similar changes, but believes the duodenum to be involved most often. The lymphoid hyperplasia

appears to have been much less pronounced in his cases than in our series. Hemorrhagic gastro-enteritis has been described (Juergens,[49] Wallis,[24] Windgradow[50]).

Nervous System.—The brain and its membranes were examined in eighty-five cases, and next to the diseases of the respiratory apparatus, the changes in the nervous system seem to be the most frequent and important complications in influenza.

Dura Mater.—Congestion, generally of a mild degree, was found in twenty-nine instances. In one case a marked internal hemorrhagic pachymeningitis occurred in conjunction with a purulent meningococcic meningitis. The entire inner surface of the dura was coated with a thick layer of firmly clotted blood, averaging from 2 to 5 mm., which adhered but slightly to the pia-arachnoid, but was firmly affixed to the dura. Kuskow[2] and Leichtenstern[1] have each reported a similar case. In a general way it may be said that the dura was much less affected than the pia-arachnoid.

Pia-Arachnoid.—The relative frequency of meningitis as a complication of influenzal pneumonitis is emphasized by Gmeiner,[51] who found it in 11 per cent. of his cases, while in ordinary croupous pneumonia it occurred in 0.5 per cent. Blanton and Irons[10] saw two cases of pneumococcic meningitis in their 123 postmortems. Symmers[11] saw one such case in twenty necropsies. Nuzum[21] and his associates found passive hyperemia of the pia-arachnoid and edema of the leptomeninges commonly present in their forty necropsies. Wallis,[24] Kuskow[2] and others found similar conditions. Suppurative inflammation during and after influenza was frequently observed in the military hospitals of France and Algiers by Kelsch and Antony[32] fifteen times in 278 cases, and Kundrat[30] thrice in 126 necropsies. Kuskow[2] found only one case of purulent meningitis. He estimates its frequency during the epidemic of 1889-1890 as from 2½ to 5 per cent., and concluded that the pia is only rarely left unchanged in influenza. Similar results could be obtained for the present epidemic (Stone and Swift,[13] Blanton and Irons,[10] Nuzum and co-workers,[21] Symmers,[11] etc.).

We found fibrinopurulent leptomeningitis thirteen times, serolymphatic meningitis, with congestion, seventeen times, and in the remaining fifty-five cases edema and congestion of more or less pronounced degree. The origin of the purulent meningitis was meningococcic in seven cases, pneumococcic in four, and streptococcic in two

49. Juergens: Berl. klin. Wchnschr. No. 10, p. 232, 1890.
50. Windgradow: Quoted by Kuskow, Footnote 2.
51. Gmeiner: Einige Beobachtungen über Influenza Während der letzten Epidemie, Prager med. Wchnschr., 1894; ibid. 1894.

instances. Further etiologic data will be given in the bacteriologic part of this paper. The constantly present congestion and edema doubtless created a focus of lessened resistance, explaining the frequency of meningeal complications. The frankly purulent inflammations generally occurred late in the disease, but some developed within a few days after the onset of the influenza. They differed anatomically in no way from the usual lesions of this type. The other meningeal infections which we have here termed serolymphatic appear to be the direct result of the virus of influenza. In all of these cases the membranes were soft, watery and considerably congested.

The subarachnoid fluid, especially in the large cysterns, was definitely turbid. In the sulci and surrounding the larger vessels, there

Fig. 35.—(Pia-arachnoid.) Acute serous leptomeningitis. Note distention with poorly cellular exudate and congestion. This is an early stage of the condition shown in Figure 36.

was a cloudy, turbid, grayish yellow exudate. This was most frequently observed over the temporal and parietal regions, and was slight or absent over the base of the brain. Microscopically, two types were recognized. In the first (Fig. 35) the pia-arachnoid was loosely arranged and distended with fluids, the vessels were densely filled. Isolated red blood cells and small round lymphatic cells were scattered throughout the tissue with occasional large endothelial cells. In the second type (Fig. 36) the pia-arachnoid was densely infiltrated with small round, many large, deep-staining mononuclear, some pale-staining

endothelial together with plasma cells. Polymorphonuclear leukocytes were rarely encountered, and then in small numbers; fibrin was absent, or at most only present in small traces. This type of meningitis was characterized, then, by the lymphocytic type of the cellular exudate and the scarcity or absence of polymorphonuclear cells and fibrin, together with pronounced hyperemia, edema and occasional hemorrhages.

Brain.—The weight of the brain was tabulated for forty-six cases. In 39 per cent. it averaged 1,300, in 50 per cent., 1,452; in 11 per cent., 1,739 gm. The weight, therefore, was increased from 100 to 200 gm. in about half of the patients. Consistency was somewhat more flaccid. The ventricles were generally of normal size, or only slightly dis-

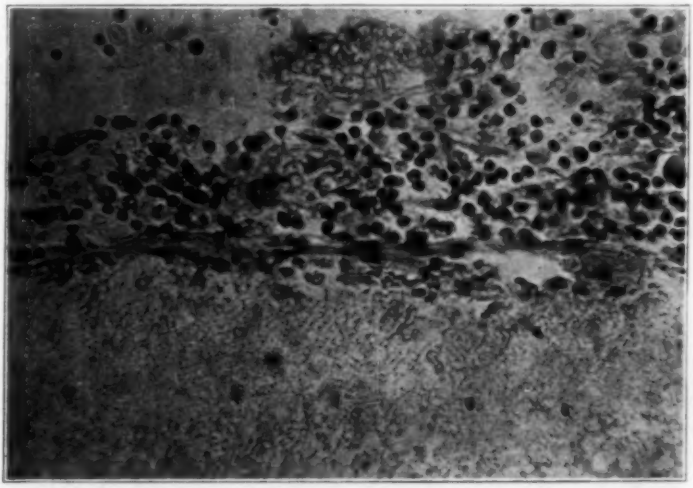

Fig. 36.—(Pia-arachnoid.) Acute serolymphatic meningitis. The exudate consists of numerous small, round cells, many large, deeply staining mononuclear cells, and plasma cells. Polymorphonuclear leukocytes are very rarely encountered, and fibrin is only present in small traces.

tended. Slight cloudiness of the ventricular fluid was often observed, even in the cases not associated with purulent meningitis. The ependyma presented no noteworthy alteration. The pineal gland was grossly normal, or at the most, somewhat softened. No microscopic studies of them are included in this series. The cut surfaces of the brain in practically every instance, presented an excessive number of bleeding points. They were most pronounced in the white matter of the hemispheres, but occasionally the corpus thalamus was especially involved. The cerebral cortex was less affected and the pons, cere-

bellum, medulla and spinal cord presented these changes in considerably less degree. These bleeding points appeared usually as closely placed, punctate, minute, hemorrhagic areas.

Microscopically, intense congestion of the vessels and numerous minute hemorrhagic foci were encountered (Fig. 37). Their distribution corresponded to the grossly hyperemic areas. The hemorrhages never exceeded, in size, the diameter of a low power microscopic field and were generally only of about half this size. The hemorrhagic encephalitis was first studied by Leichtenstern;[1] Schmorl[52] and Oberndorfer,[27] saw it frequently during the present European epidemic. Pick[7] and Leichtenstern,[1] occasionally found areas of hemorrhagic

Fig. 37.—(Cerebrum.) Focal hemorrhages and congestion. Note area of hemorrhage in upper right part of photograph.

softening of considerable extent; such areas did not occur in our series. The vascular endothelium was frequently swollen and hyaline and conglutination thrombi were often met. The perivascular spaces were frequently large and contained precipitated, edematous fluid. Occasionally, only, was a perivascular cellular infiltration noted (Fig. 38). The ganglion cells presented most pronounced changes. Some-

52. Schmorl: Path.-anat. Beobachtungen bei d. jetzt herrschenden Influenza Epidemie, Deutsch. med. Wchnschr. **44**:936, 1918.

times only isolated, sometimes large groups of cells, were affected. They were generally swollen and without definite cell outline. Commonly, a small, clear, edematous zone surrounded the cells. The cytoplasm was devoid of Nissl granules and the nuclei were frequently entirely absent or showed a loss of outline. In short, all stages of cell degeneration were present, ranging from acute cloudy swelling to chromatolysis and total disappearance (Fig. 39). In no instance, however, was invasion and phagocytosis of ganglion cells observed. The glia matrix was generally arranged loosely. The cell degenerations enumerated did not appear to attack constantly any special part of the brain, and the sections of spinal cords examined were too few to formulate an opinion.

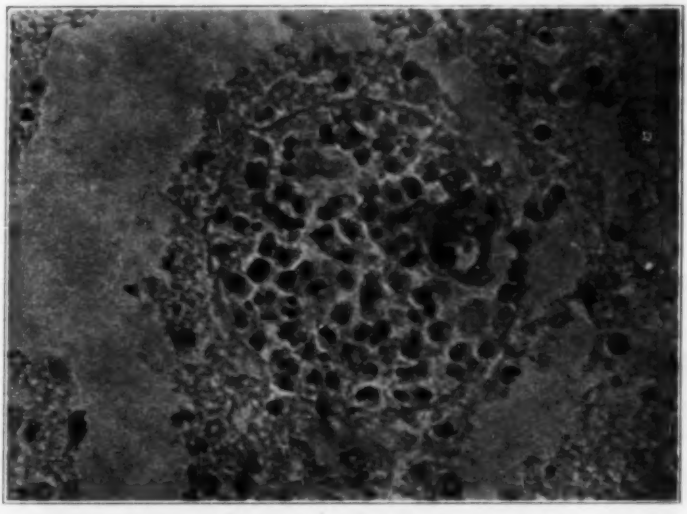

Fig. 38.—(Brain.) Perivascular cell infiltration. Note the huge distention of perivascular space with polymorphonuclear leukocytes and large mononuclear cells. The darker small circle within the polymorphonuclear mass is the vessel; the polymorphonuclear cells occupy the perivascular space. This was taken from a case of influenza complicated with suppurative meningitis. Polymorphonuclear cells are generally only met with in influenza when complications due to pus producing organism exist. Compare this with Figure 36, where the perivascular space is free from cellular contents.

Pituitary Gland.—This gland was only examined a few times. In each instance it was somewhat swollen, pinkish in color, the cut surface being moist, definitely bloody and reddened. Microscopically, the tubular acini were markedly distended with a colloid material, the

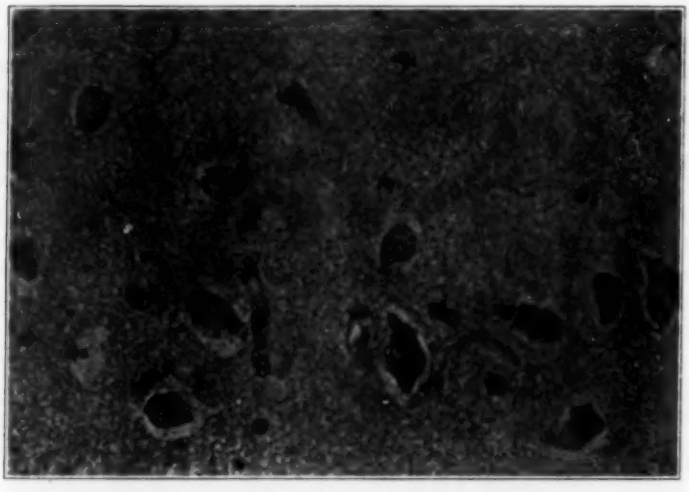

Fig. 39.—(Cerebrum.) Acute cloudy swelling and degeneration of ganglion cells. Note clear area of edema, surrounding ganglion cells, absence of tigroid granulation, and nuclear changes, varying from eccentric position of nucleus to partial and complete chromatolysis.

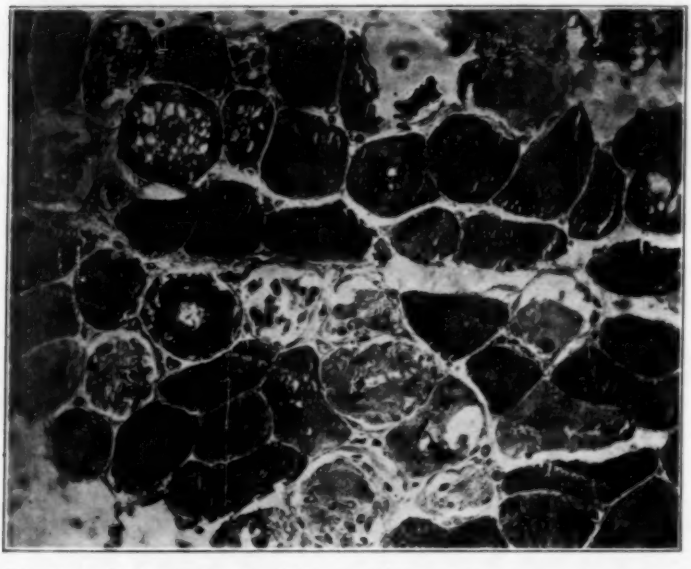

Fig. 40.—(Pituitary gland.) Hypercolloidism. Note the marked distention with colloid material.

lining cells flattened; sometimes throughout the section coarse strands of fibrin were present. The vessels were much dilated and small hemorrhages were frequently seen. The posterior lobe was unfortunately never included in the sections. These unusual findings are readily explained by the great frequency of purulent nasal sinus involvement and by the frequent association of suppurative meningitis. The section illustrated here came from a patient presenting suppuration of the sphenoid and other accessory nasal sinuses, but the meninges were not inflamed (Fig. 40).

Special Sense Organs.—Ear: Suppurative otitis media was present in only four instances. This stands in marked contrast to the frequency with which it occurred during a coexisting epidemic of measles where it was present in nine of twenty-five necropsied patients. During the epidemic of 1889 and the succeeding years the relative infrequency of middle ear involvement was noted. Thus, the Swiss Commission[53] found it in only 2 per cent. of 1,508 cases. Leichtenstern[1] gives similar figures.

Eye: Hyperemia and inflammation of the conjunctiva were very frequently found and would probably indicate the generalized vascular engorgement rather than a localized condition. No microscopic sections of the eyes were made.

CHRONIC INFLUENZA

While influenza, as a rule, runs an acute course, it may become protracted over a considerable period. This condition has been especially studied by Lord,[54] Filatoff,[55] Franke[56] and others. Any case of influenza which extends over a period of four weeks or more, generally with remittent or intermittent fever, and various lung symptoms, may be looked on as typical of the chronic form of this disease. The authors mentioned, and others, state that clinically such a condition often resembles typhoid, malaria, tuberculosis, or low grade septicemia. These "subacute and chronic nontuberculous pulmonary infections" have lately been reviewed by Miller.[57]

Five patients of our series of 126 presented this condition. The duration of the disease varied from 44 to 88 days, with an average of 60 days. Judging from the clinical records, each patient suffered with

53. Swiss Commission: Quoted by Leichtenstern, Footnote 1.
54. Lord, F. T.: Boston M. & S. J. **147**:662, 1902; ibid. **153**:537, 1905.
55. Pilatoff, N.: Ueber Protrakierte u. Chron. form d. influenza, Arch. f. Kinderheilk. **27**: 1889.
56. Franke, Felix: Ueber Chronische Influenza, Beihefte zur med. Klin., Berlin **5**: 1909.
57. Miller, Alexander: Subacute and Chronic Nontuberculous Pulmonary Infections, Am. J. M. Sc. **154**:805, 1917.

an initial typical attack of influenza, which was followed, sooner or later, by signs of pneumonic consolidation and accompanied throughout by a fluctuating fever curve. The pneumonitis seemed to persist, but shifted from place to place, constantly involving new areas, while the older pneumonic patches persisted or sometimes cleared up.

All these cases came to necropsy during the last period of the epidemic, or rather after the bulk of the epidemic had subsided. They showed certain anatomic differences which justify their separate discussion.

There was emaciation in each instance, two showed slight icterus, none the intense cyanosis and lividity so commonly seen in the acute cases. The cut surface of the subcutaneous tissues and muscles was never so bloody and moist as in the acute disease. In one instance a large abscess in the rectus muscle was present. Acute purulent peritonitis occurred thrice, which is in marked contrast to its absence in the acute cases of our series. The changes in the aorta and other vessels were similar but more profound.

Pericardium and Heart.—Purulent pericarditis, associated with a purulent inflammation of the other serous membranes, was present once. In the rest no noteworthy changes were found. There was particularly an absence of subserous, hemorrhagic extravasations and of hyperemia.

The heart varied in weight from 205 to 425 gm., with an average of 310 gm. The right heart was constantly dilated, and in one instance both chambers were markedly dilated. The muscle was always very flaccid, light grayish red and turbid.

Microscopically, there was shown marked swelling and vacuolization of hydropic character, and while the vessels were not congested, usually they contained hyaline thrombi, which were more pronounced in the chronic than in the acute cases. Endothelial hyperplasia varied in degree in the chronic form, and no definite comparative picture could be formed.

Respiratory Tract.—The peribronchial lymph nodes were always greatly swollen, soft and edematous, but only slightly congested. Microscopic section presented edema, sinus catarrh, slight connective tissue proliferation, and, in two instances, an acute purulent adenitis, with the presence of large numbers of polymorphonuclear leukocytes and small areas of necrosis. The vessels showed no other changes than those mentioned above.

The trachea and bronchi possessed a relatively pale mucosa which was covered in every instance with mucopus; in the smaller branches a thick, creamy, yellow pus was present. Microscopically, well marked

erosion of the wall, and the presence of enormous numbers of polymorphonuclear cells characterized the picture. Bronchiectasis never occurred, although commonly seen in chronic influenza.

The pleurae, in each instance, were adherent in places by relatively firm, fibrous bands and by more recent fibrinous exudate. This seemed to have persisted for some time, since it was generally rather tough. The pneumonic process, according to the records, varied in duration from twenty-seven to seventy-four days with an average of 44.1 days. The lungs were never so voluminous as in the acute type, and in no instance exceeded the volume usually seen in a chronic bronchopneumonia, the left lung averaging 440, the right 480 gm. in weight. Slaty blue, sometimes depressed, firm areas could be felt, especially on the posterior border in either lung. The cut surface was only slightly bloody, and in every instance the interpulmonary septa were prominent and there were larger and smaller areas of fleshy appearance and consistency. Soft, grayish brown foci, finely and coarsely granular, apparently recent consolidations, and smooth, velvety, firm areas could be seen, but in general the extent of pulmonary involvement was less than in the acute cases.

Microscopically, certain characteristic features were always present; namely, areas of atelectasis, sometimes of considerable extent; areas of young connective tissue overgrowth (carnification) and areas of necrosis and abscess formation. All stages of pneumonic involvement could be observed in the sections from these lungs. In every instance small, bronchopneumonic patches, with fibrinocatarrhal exudate of recent origin, were found. Generally, however, the exudate consisted of polymorphonuclear leukocytes, with little or no fibrin; the alveolar walls were infiltrated in places with such cells, and were frequently destroyed, resulting in abscesses which often reached considerable dimensions. The perivascular and peribronchial tissues were often definitely fibrous. In one instance a pronounced hyperplasia of epithelium, similar to that described in acute cases, was encountered.

Spleen.—The spleen varied in weight from 105 to 260 gm., with an average of 185 gm.; on the whole, the organ was therefore smaller than in the acute cases. The capsule was generally wrinkled; the color of the organ was a reddish gray; the consistency was always flaccid, but never soft or mushy. The cut surface was only slightly bloody; trabeculae could generally be seen, but were not thickened. In one case the follicles were prominent, in the others indistinct.

Microscopically, there was a distinct hyperplasia of endothelial cells throughout the organ; in two instances large numbers of polymorphonuclear leukocytes were present. Fibrosis of the reticulum was noted

twice. Definite toxic hyaline degeneration of the arterial walls was noted in another case. Areas of hemorrhage were seen twice.

Suprarenals and Semilunar Ganglia.—Slight congestion and edema were observed. In one instance there was infiltration of the adrenal with polynuclear leukocytes, otherwise the changes were similar to those previously described.

Kidneys.—Twice the kidneys were below average weight, and three times increased in size and weight, the average for the series being 193 gm. for the left and 190 gm. for the right kidney. In two cases the capsule was slightly adherent, tearing the parenchyma on stripping. The consistency in every instance was flaccid; the cut surface was pale, swollen and reddish gray, with poor differentiation of cortex and medulla. Cortical and medullary markings had a washed-out appearance. Hemorrhagic exudates in the renal pelvis were never observed.

Microscopically, there was a slight edema and congestion present in all, but no connective tissue overgrowth. The glomerular and tubular changes were similar to those described, differing only in greater degree of severity. In one instance polymorphonuclear leukocytes in large numbers were present in the glomerular capillaries; in another case the capsular epithelium was slightly proliferated. The tubular epithelium was considerably more degenerated than in the acute cases; many tubules were lined with entirely necrotic cells.

Liver.—Two cases were below the average in weight (1,330 gm.), the other three averaged 2,270 gm. The consistency was flaccid in each instance, the lower border well rounded. The color was generally grayish brown. The cut surface was slightly bloody, lobulation was indistinct, but sometimes the centers of the lobules were large and deep red.

Microscopically, the two small livers presented marked degeneration of cells, areas of focal necrosis and a diffuse infiltration of polymorphonuclear cells which latter was somewhat more marked in the periportal tissue. In the other organs varying degrees of cloudy swelling were observed.

Meninges and Brain.—The dura mater presented no changes. The pia-arachnoid was twice slightly edematous, and in one case of the three examined the vessels were considerably congested. Much opacity was present in this case, and over the superior surface of the cerebellum there was a small amount of grayish yellow exudate. This patient had shown symptoms of spinal meningitis for about one month, but repeated lumbar punctures failed to bring out the causative organism.

Microscopically, there was a round cell infiltration with few leukocytes and some fibrin. The brain weight in the three cases averaged 1,480 gm. Only once did the cut surface show the marked congestion and petechial hemorrhage described above, while in the other two no gross changes were noted. Microscopically, there were degenerative changes in the ganglion cells similar to those already described; hemorrhages were never found.

SUMMARY

The influenza pandemic of 1918 manifested itself at Camp Zachary Taylor and Camp Knox, Kentucky, Sept. 22, 1918, and terminated about November 15. One hundred and twenty-six definitely proven cases of influenza, occurring in previous healthy soldiers of approximately the same age and physical condition, were chosen for this study. One hundred and twenty-one of these cases represented the acute, five the chronic type of the disease. All stages of the epidemic are covered. Routine bacteriologic cultures were made in every instance.

Considerable discrepancy was found in the morbidity and mortality rates between white and negro soldiers, the incidence of influenza being considerably less among the colored soldiers, while their mortality was higher.

The average duration of life was found to be fourteen days; about 50 per cent. of the patients died within ten days. There was a tendency for the duration of the disease to increase as the epidemic progressed.

The external appearance of the necropsied cases usually presented an extreme lividity. Expansion of the chest was frequently found.

Skin.—Two types of skin lesions were encountered. These were purpura hemorrhagica, in about 20 per cent., and toxic necrosis of the sebaceous follicles in about 60 per cent. of the cases. Jaundice was present in about 10 per cent.

Subcutaneous Tissues. — Generalized emphysema was present in three cases. We believe the mode of origin of this to lie in ulcerative or erosive bronchiectasis with escape of the air in the peribronchial tissue and thence to the mediastinum and subcutaneous tissue.

Muscles.—Zenker's hyaline degeneration of the rectus muscles was observed in about 10 per cent. of the cases. Acute myositis occurred once. Abscesses occurred once each in the acute and chronic cases.

Peritoneum.—Peritonitis occurred in none of the acute and three times in the chronic cases.

Blood Vascular System.—Extreme congestion, areas of hemorrhages, conglutination and hyaline thrombosis, and swelling of the

vascular endothelium was commonly present. Rarely was a toxic hyaline degeneration of the arterial wall seen. Polymorphonuclear leukocytes were only found in complicating suppurative processes; their absence seemed to indicate a myeloid intoxication. Lymphoid hyperplasia was, on the other hand, often very pronounced.

Aorta.—Slight acute atheroma was present in about 85 per cent. of the cases; diffuse hemoglobin tinting of the intima was frequently observed.

Pericardium.—Pericarditis occurred seven times. Punctate hemorrhagic extravasations and hyperemia were common.

Heart.—The heart muscle was practically always affected. In over 90 per cent. of the cases more or less relaxation of the right heart was present; in over 80 per cent. an associated cloudy swelling occurred. Microscopically, there was an acute parenchymatous degeneration and vacuolization. Endocarditis was seen only once.

Respiratory System.—The respiratory mucosa was generally somewhat swollen and frequently hemorrhagic. The accessory nasal sinuses presented purulent or sanguinopurulent involvement in about 85 per cent. of the cases. The peribronchial lymph nodes were generally congested, enlarged and edematous. Microscopically, an acute sinus catarrh was almost always present. The larynx was involved in about one-third of our cases, while the trachea and bronchi presented a hemorrhagic or catarrhal mucosa in almost every instance. Ulcerative and purulent bronchiolitis was very common.

Pleurae.—The pleurae were involved on one or both sides in over 80 per cent. of the cases. The exudate was generally slight in amount, frequently hemorrhagic and usually poor in fibrin. Analysis in reference to the duration of the disease and period of epidemic brought out the fact that purulent and the more pronounced fibrinous fluids occurred at a later stage of the epidemic. Petechial subpleural hemorrhages were very frequent.

Lungs.—Pneumonitis developed usually early. All but two cases presented pneumonic involvement, but the amount of lung involvement was occasionally so slight that it was evidently not the cause of death. In over 90 per cent. of the cases both lungs were involved. The lung was generally much above normal weight. The pneumonitis was generally lobular in type, true croupous lobar pneumonia occurring in only thirteen instances. In seven of these it formed the only type of pulmonary consolidation; in six others it was associated with bronchopneumonia. The bronchopneumonic areas varied considerably in texture, color and consistency, were usually poorly circumscribed, and tended to become confluent. The upper lobe was almost as frequently

affected as the lower. The nonconsolidated lung tissue was generally very hyperemic. Microscopically, three types of exudates were differentiated: catarrhal, fibrinocatarrhal, and fibrinopurulent. All of these often occurred within the same lung, or even in the same microscopic section. The catarrhal types of exudates appeared to be primarily produced by the virus of influenza, while the fibrinous and purulent types were probably the results of secondary and tertiary invading organisms. The essential pathology of true influenzal pneumonitis seemed to be the extreme hyperplasia of the pulmonary epithelium, but since invading organisms were generally abundant a mixed catarrhal, fibrinous and suppurative pneumonitis was generally encountered.

Spleen.—The spleen was definitely enlarged in over 80 per cent. of the cases and considerably enlarged in 30 per cent. It was usually flaccid, occasionally mushy and generally bloody. Trabeculae were rarely recognized distinctly. Follicular enlargement was uncommon. Necrosis of the reticulum, endothelial hyperplasia, and toxic hyaline degeneration of arterial walls and germinal centers were frequently found.

Semilunar Ganglia.—Marked changes in the ganglion cells, varying from cloudy swelling to complete disappearance were prominent. Hyperemia was usually present.

Suprarenals.—The adrenals were usually congested and somewhat edematous, and in three cases a frank hemorrhage was present. Lipoid exhaustion was the most notable change.

Kidneys.—The kidneys were generally enlarged, flaccid and congested. The tubular lumen and capsular spaces contained abundant granular precipitate. The tubular epithelium was degenerated and sometimes necrotic. Proliferation of the capsular epithelium occurred occasionally. The kidney changes seemed to be in the nature of a parenchymatous degeneration with edema rather than of a productive nephritis.

The genital organs were frequently congested. Cellular degeneration and absence of spermatogenesis were commonly found.

Upper Gastro-Intestinal Tract.—Submucous hemorrhages were frequent. A moderate lymphoid hyperplasia was present.

Liver.—The liver was definitely increased in size and weight in over 90 per cent. Cloudy swelling, with various stages of congestion, were common. Focal necrosis was present in about 50 per cent. of the cases. In one instance a true acute yellow atrophy was encountered, and in several more necrotic changes which could be looked on as precursors of yellow atrophy.

Pancreas. — Toxic degeneration of the islands of Langerhans occurred with great frequency.

Intestines.—The solitary follicles and Peyer's patches were as a rule definitely enlarged. Congestion and submucous hemorrhages were often found.

Brain Membranes.—The dura mater was congested in about one-third of the cases. Once a marked internal hemorrhagic pachymeningitis occurred. The pia-arachnoid was practically always involved. Suppurative meningitis, due to secondary invaders, was present in 20 per cent. A serolymphatic leptomeningitis, characterized by a slight exudate of cells belonging to the lymphocytic type and by absence of polynuclear cells and fibrin, was encountered in one-third of the cases. Edema and hyperemia were practically always present.

Brain.—The brain was generally congested, hyperemia and focal hemorrhages being very frequent. Degeneration of ganglion cells was pronounced. The changes were more marked in the cerebrum, while the cerebellum, medulla, pons and spinal cord showed relatively slight alterations.

Pituitary. — A marked hypercolloidism was obesrved. Fibrinous inflammation, extending from the neighboring suppurating sinuses, occurred.

Ear.—Suppurative otitis media was present in only 3 per cent. of the cases. Bone necrosis was not observed.

Eye.—Hyperemia and conjunctivitis were common.

CHRONIC INFLUENZA

In five of our cases the duration of the disease averaged sixty days. These were regarded as cases of chronic influenza and presented certain characteristic features. All of the patients were markedly emaciated. The intense postmortem lividity encountered in the acute cases was absent. The serous membranes were frequently involved. Thus, pericarditis was present in one case, and peritonitis in three instances, with a partially organized pleural exudate in every case. The organs generally presented more pronounced parenchymatous degenerations, but hemorrhages and marked congestions were absent. The heart always showed cloudy swelling and hydropic degeneration. The lungs evidenced pneumonic processes of long standing, the average duration being forty-four days. Fibrosis, carnification, atelectasis and abscesses were common, but there were always recent fibrinocatarrhal areas. The spleen was generally smaller than in acute cases, and in two instances contained large numbers of polynuclear cells. The changes in the suprarenals and semilunar ganglia were similar to those encoun-

tered in acute cases. The kidneys presented pronounced glomerular tubular nephritis. In two instances an acute suppurative hepatitis with numerous focal necroses was present. Meninges and brain showed degenerative changes similar to those found in the acute cases, but the vascular changes were slight.

BACTERIOLOGIC PART

From the inception of the epidemic at Camp Zachary Taylor it was our routine to take cultures from the principal tissues at each necropsy —heart's blood, pericardium, right and left pleurae, right and left lungs (all lobes), spleen, bronchial exudate, nasal accessory sinuses, subarachnoid space and ventricles, and elsewhere as occasion demanded.

Besides cultures, routine smears were made to act as a check on cultural findings. In our charts only cultural readings have been submitted, and this has undoubtedly lowered some percentages, but it did not seem fair to report only on staining affinity and morphologic grounds.

The reports, both pathologic and bacteriologic, of the present pandemic, as shown in the literature to date, reveal such an appalling divergency in conclusions, such diversity in reading results and in the means employed to get those results, that we are constrained to analyze our findings in comparison with those from cases not to be considered as due in any degree to the prevailing epidemic, in order to see if there were not some underlying principles governing what appeared to be a disordered mélange in the organisms found.

As a preliminary it would seem fair to state what is meant when we say we have found a particular organism. The necessity for this is shown by the fact that certain observers have regarded as pneumococci, organisms which are gram-positive diplococci whether bile soluble or not, and some have typed with pneumococcic antisera bile insoluble organisms. In this series we regarded the bile solubility test as final; a diplococcus or diplostreptococcus, whether capsulated or not, whether lanceolate or not, if bile insoluble was regarded as a streptococcus, either hemolytic or nonhemolytic according to a predetermined estimate of hemolysing ability. Frequently we encountered pneumococci agglutinating with two or more of our type antisera; these were properly regarded as Type IV. Some observers have reported the absence of the *B. influenzae,* and in their culture media they have taken no regard of its hemophilic propensities; the criteria we have demanded are mentioned below.

The gradations between hemolytic and nonhemolytic streptococci are so fine and indistinct that we had to adopt a standard of differentiation and arbitrarily chose the ability of an 18 hours' broth culture

to produce hemolysis with equal parts of a 5 per cent. sheep suspension in the water bath at 37.5 C. for two hours. The amount of the hemolysis, whether complete or not, was not considered. Some strains would give complete hemolysis in half an hour or less, while others would not cause complete hemolysis in the two hours, but an evident hemolysis, however slight, at the end of our time period was sufficient to enable us to make a differentiation. All tests were run with two saline controls. The hemolytic streptococci were again subdivided in a number of instances by the Holman[58] sugar standard. By this means we determined the curious fact that *S. pyogenes,* which had so abounded at Camp Zachary Taylor in 1917-1918 (reports by Lucke and Rea,[59] and by Alexander,[60] Camp Taylor) is not represented among those found this year, its place being taken by hemolytic streptococcus No. 2. Double tests with fresh sugars were taken and corroborated these findings. Fifty strains of streptococcus were examined with the following results:

Hemolytic streptococcus:	Per cent.
No 2	70.3
No. 1	3.7
No. 3	7.4
Equinus	11.2
Infrequens	7.4

Nonhemolytic streptococcus:	Per cent.
Equinus	45.5
Ignavius	22.7
No. 2	11.3
Mitior	11.3
Salivarius	11.3

This hemolytic streptococcus No. 2 was very frequently gram-negative, not taking the Gram stain after repeated cultivation. It was recovered at one time or another from practically every organ or tissue, and on two occasions from the spinal fluid.

By the *B. influenzae* we mean a minute organism, gram-negative, pleomorphic, hemophilic, which would not grow at room temperature, or only very slightly, and was generally killed by icebox temperature. As a medium we used for a time rabbits' blood glycerin agar, the growth appearing as multitudinous dewdrop colonies in from 20 to 48 hours. With the Washington formula the colonies were much larger, ringed and diverse in size and contour, giving a false impression of contamination. More latterly we have used Avery's[61] oleate

58. Holman, W. L.: The Classification of Streptococci, J. M. Res. **34**:377 (July) 1916.

59. Lucke, Baldwin, and Rea, Marion: Hemolytic Streptococci, etc., J. Infect. Dis., 25, May, 1919.

60. Alexander, H. L.: Hemolytic Streptococcus Causing Severe Infections at Camp Zachary Taylor, Ky., J. A. M. A. **70**:775 (March 16) 1918.

61. Avery, Oswald T.: J. A. M. A. **71**:2051 (Dec. 21) 1918.

medium with very gratifying results. Agglutination experiments of our cultures against serum from recovered cases were doubtful or unsuccessful, except in two instances where we get the following results after incubation at 55 C. for eighteen hours followed by twelve hours in the icebox:

1:2	1:10	1:20	1:40	1:80
++	++	++	+	±

Under the head of *Micrococcus catarrhalis* we include all members of this group, hardly any attempt at sugar or other differentiation having been made in the time at our disposal. Latterly, though, we have found a prevalent diplococcus, both in sputum and at necropsy, the colonies resembling the *Micrococcus catarrhalis,* but morphologically showing slight differences. Since it fermented dextrose, saccharose and lactose we have considered the possibility of it being *Micrococcus crassus.*

With these preliminary explanations we here submit our charts.

TABLE 8.—Comparative Incidence of Bacterial Flora in One or More Organs of 120 Necropsies of Influenza, and 101 Other Acute Diseases Occurring During the Influenza Epidemic

	Heart's Blood				All Organs			
	Influenza (107)		All Other Diseases (101)		Influenza (120)		All Other Diseases (101)	
	Number	Per Cent.	Number	Per Cent.	Number	Per Cent.	Number	Per Cent.
B. influenzae	30	28.0	4	3.9	74	61.6	22	21.7
Hemolytic streptococcus	32	29.9	32	31.6	41	34.1	51	50.4
Nonhemolytic strept.	31	28.9	10	9.9	56	46.6	18	17.8
Pneumococci (typed)	24	22.4	5	4.9	43	35.8	11	10.8
Pneumococci (untyped)	6	5.6	5	4.9	25	20.8	12	11.8
M. catarrhalis	3	2.8	1	0.9	35	29.1	11	1.1
Meningococcus	0	0.0	0	0.0	2	1.6	4	3.9
M. tetragenus	0	0.0	1	0.9	6	5.0	2	1.9
Staphylococcus	2	1.8	5	4.9	18	15.0	30	29.7
Diphtheroids	0	0.0	0	0.0	6	5.0	0	0.0

In Table 8 we make a comparison of the bacterial findings from 120 influenzal with those from 101 necropsies from other causes. These deaths all occurred during the period under consideration and should give a fair line, if such is to be obtained, on the leading bacterial factors in the epidemic seen at Camp Zachary Taylor. It will be seen that four organisms especially predominated in the influenza cases; these were *B. influenzae,* a nonhemolytic streptococcus, pneumococcus of the various types, and *M. catarrhalis.*

The presence of the Pfeiffer bacillus in the heart's blood of 3.9 per cent. of the noninfluenza cases is to be explained by the fact that there

was a concurrent epidemic of measles, and these cases in a high percentage carried an organism indistinguishable from the *B. influenzae*, judging from a series of nasopharyngeal swabbings. The hemolytic streptococcus was not found in so high a percentage as in the noninfluenzal cases, and it was only at the latter end of the epidemic, and in those cases which were protracted, that it was met with to any considerable extent; so that we have been inclined to look on it as a tertiary invader, in view of the fact that it has been endemic in this camp for the past eighteen months. The other organisms mentioned on this chart need not now be considered.

The outstanding prominence of the *B. influenzae* is very noteworthy, and when the difficulty of its isolation and the fact that in the long continued cases it seems to have died out or been replaced by the secondary or tertiary invaders, it is evident that these figures can only represent the minimum number of times it was present during some period of the disease. In only two of our series did we have a pure infection with this organism, and these were very early in the epidemic. Early also were eight cases of mixed infection with *B. influenzae* and a nonhemolytic streptococcus, and three of *B. influenzae* pneumococcus; eight cases scattered throughout the epidemic of pure nonhemolytic streptococcus. Midway was one of pure *M catarrhalis;* ten cases mostly at the very end of pure hemolytic streptococcus, and eight cases in this last period of mixed hemolytic streptococcus and staphylococcus. Nonhemolytic streptococcus and pneumococcus were found about three times as often in the influenza as in the noninfluenza cases. *M. catarrhalis* was very prominent in the latter part of the middle of the epidemic.

One very interesting organism encountered was a small biflagellated protozoon, measuring from 5 to 8 microns, and without undulating membrane, tentatively assigned to the Prowazekia. This was discovered in three cases close together toward the middle of the epidemic. In one instance it was recovered from the heart's blood; in another from the sphenoid sinus, and in the third from the left lung. A later notice on this organism will be issued when it has been more thoroughly studied.

Table 9 gives the incidence and distribution of the bacteria according to the period of the epidemic. We have divided the epidemic into four time periods, the dates being given in Table 2, except that periods 4 and 5 of this table are consolidated here and constitute period 4 in Table 9. For sufficient reason we have amalgamated the readings of the right and left pleurae, right and left lungs, the accessory nasal sinuses and mastoid cells. By "other structures" are meant liver,

TABLE 9.—Incidence and Distribution of Bacteria, According to Period of Epidemic (in Per Cent.)

	Organs																													
	Heart's Blood				Pleurae Right 41 Left 43				Lungs Right 116 Left 117				Bronchial Exudate				Spleen				Subarachnoid and Brain Ventricles				Accessory Nasal Sinuses and Mastoid Cells				Other Structures			
	Period				Period				Period				Period				Period				Period				Period*				Period			
	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
No. of examinations	41	30	16	33	45	21	7	11	82	60	32	59	16	22	9	4	37	28	14	31	16	26	17	9	24	42	15	18	26	15	4	8
B. influenzae	48.7	3.3	6.2	24.2	20.0	19.0	0	0	54.8	25.0	37.5	3.3	50.0	36.3	66.6	0	48.3	10.7	25.0	0	6.2	11.5	17.6	0	33.3	30.9	46.6	0	34.6	13.3	50.0	0
Hemolytic streptococcus	21.9	10.0	6.2	54.4	26.6	9.5	14.2	54.5	26.8	15.0	6.2	54.2	18.7	18.1	0	50.0	10.7	10.7	0	22.8	0	3.8	5.8	44.4	4.1	9.5	6.6	38.8	3.8	6.6	50.0	62.5
Nonhem. streptococcus	26.8	50.0	18.7	6.0	22.2	42.8	85.7	9.0	45.1	45.0	37.5	15.2	3.7	45.4	22.2	0	19.1	32.1	21.4	5.4	31.2	30.7	5.8	11.1	45.8	40.4	20.0	11.1	19.2	6.6	25.0	0
Pneumococcus, total	21.7	26.4	37.4	18.0	24.2	52.2	42.7	9.0	41.7	49.7	46.7	19.9	24.9	58.7	55.5	0	10.8	28.3	7.1	16.0	6.2	38.2	35.0	22.2	24.8	49.7	39.8	27.6	3.8	39.8	50.0	12.5
Pneumococcus, Type I	2.4	3.3	0	3.0	0	9.5	0	0	4.8	6.6	0	3.3	0	9.0	0	0	0	7.1	0	3.2	0	0	0	0	0	2.3	0	5.5	0	6.6	0	0
Pneumococcus, Type II	4.8	6.6	0	3.0	2.2	0	14.2	0	3.6	5.0	6.2	6.7	0	4.5	0	0	2.7	7.1	0	0	0	11.5	5.8	0	0	7.1	0	11.1	0	6.6	0	0
Pneumococcus, Type IIa	4.8	6.6	0	0	6.6	9.5	0	9.0	3.6	6.6	3.1	0	6.2	9.0	11.1	0	2.7	3.5	0	3.2	0	7.6	5.8	0	12.4	4.7	6.6	0	0	18.3	25.0	0
Pneumococcus, Type III	0	0	6.2	3.0	0	0	0	0	1.2	1.6	6.2	3.3	0	0	11.1	0	0	0	0	3.2	0	0	5.8	22.2	0	0	6.6	5.5	0	0	0	0
Pneumococcus, Type IV	2.4	6.6	25.0	6.0	6.6	19.0	28.5	0	3.6	18.3	25.0	5.0	12.5	27.2	22.2	0	2.7	7.1	7.1	6.4	0	11.5	17.6	0	4.1	21.4	26.6	5.5	0	0	25.0	12.5
Pneumococcus, untyped	7.3	3.3	6.2	3.0	8.8	14.2	0	0	16.9	11.6	6.2	1.6	6.2	9.0	11.1	0	2.7	3.5	0	0	6.2	7.6	0	0	8.3	14.2	20.0	0	3.8	13.3	0	0
M. catarrhalis	0	0	18.7	0	4.4	0	14.2	0	18.1	6.6	34.3	6.7	6.2	4.5	55.5	50.0	2.7	0	25.0	3.2	0	0	5.8	0	0	2.3	20.0	5.5	7.6	6.6	25.0	0
Meningococcus	0	0	6.2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	11.7	0	0	0	13.3	0	0	0	0	0
M. tetragenus	0	0	0	0	2.2	0	0	0	2.4	0	0	0	0	4.5	0	0	0	0	0	0	0	0	0	0	0	0	6.6	0	0	0	0	0
Diphtheroids	4.8	0	6.2	0	0	0	0	0	0	3.3	0	6.7	0	9.0	11.1	25.0	0	7.1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Staphylococcus	0	0	0	12.1	0	0	0	18.1	2.4	0	0	27.1	0	0	0	25.0	0	0	0	16.3	0	0	0	22.2	0	0	0	11.1	0	0	0	12.5

peritoneum, gallbladder, skin, enteric follicles, or whatever tissue seemed to us to be worthy of examination outside of those adopted as routine. This table points out forcibly (a) the gradual lowering in the incidence rate of *B. influenzae,* nonhemolytic streptococcus and pneumococcus; (b) the sudden rise into prominence in the third period of the *M. catarrhalis,* and (c) the remarkable manner in which the hemolytic streptococcus and the staphylococcus came to the fore in the last period. The latter especially had been practically nonexistent, so far as our necropsy cultures showed during the first three periods. The sudden recurrence of *B. influenzae* in the fourth period will be discussed later.

Table 10 shows the incidence of the bacteria in the various organs. In this table is given in brackets the actual number of times each organism was found, also the resulting percentage per number of examinations made. Here again we see that the trinity, *B. influenzae,* nonhemolytic streptococcus and pneumococcus were the predominating findings in all the tissues examined. The high percentage of hemolytic streptococcus is due in most part to the very considerable frequency with which it appeared in the fourth period as above pointed out. Type IV, as elsewhere, was the principal pneumococcus found, followed by considerably less than half that number of Types IIa and II, which were almost equal in point of frequency. In this table the figures for the heart's blood are based on the total number of cultures taken, and not excluding the hopelessly contaminated, thirteen in number. If these last be taken into account, a slight increase in all the percentages would have to be recorded.

It is in line with the pathologic picture revealed at necropsy that the findings for the subarachnoid and brain ventricles were so frequently positive.

Table 11 divides our findings according to a different method; that is, according to the time the disease lasted before a fatal termination. Detailed figures have already been given in showing the relation of duration of disease to period of epidemic. Naturally, those that endured the longest came to necropsy in the later periods; so that there must necessarily be some similarity between this and the preceding table. But this table shows most forcibly the gradual disappearance of the *B. influenzae* in the longest enduring cases and the encroachment of the hemolytic streptococcus in the same. The relative infrequency of the hemolytic streptococcus in the bronchial exudate as compared with its appearance in the lungs may be due to the fact that so many more lung examinations were made, especially as toward the end of the epidemic examination of the bronchial exudate was discontinued, and at this time the hemolytic streptococcus flourished most vigorously.

TABLE 10.—Incidence of Bacteria in the Various Organs

	Organs																					
	Heart's Blood		Pleurae Right 41 Left 43		Lungs Right 116 Left 117		Bronchial Exudate		Spleen		Subarachnoid and Brain Ventricles		Accessory Nasal Sinuses and Mastoid Cells		Other Structures		Total	
Number of organs examined	(120)		(84)		(233)		(51)		(110)		(68)		(99)		(53)		(818)	
		%		%		%		%		%		%		%		%		
B. influenzae	(30)	25.0	(13)	15.4	(74)	31.7	(22)	43.1	(25)	22.7	(7)	10.2	(28)	28.8	(13)	24.5	(212)	
Hemolytic streptococcus	(31)	25.8	(21)	25.0	(65)	27.8	(9)	17.6	(14)	12.7	(6)	8.7	(13)	13.1	(9)	16.9	(168)	
Nonhemolytic streptococcus	(31)	25.8	(26)	30.9	(85)	36.4	(18)	35.2	(21)	19.0	(15)	22.0	(33)	33.3	(7)	13.2	(236)	
Pneumococcus, Type I	(3)	2.5	(2)	2.3	(10)	4.2	(2)	3.9	(3)	2.7	(0)	0	(2)	2.0	(1)	1.8	(23)	
Pneumococcus, Type II	(5)	4.1	(2)	2.3	(12)	5.1	(1)	1.9	(3)	2.7	(4)	5.8	(5)	5.0	(1)	1.8	(33)	
Pneumococcus, Type IIa	(4)	3.3	(6)	7.1	(8)	3.4	(4)	7.8	(3)	2.7	(3)	4.3	(6)	6.0	(3)	5.6	(37)	
Pneumococcus, Type III	(2)	1.6	(0)	0	(6)	2.5	(1)	1.9	(1)	0.9	(3)	4.3	(2)	2.0	(0)	0	(15)	
Pneumococcus, Type IV	(9)	7.5	(9)	10.7	(25)	10.7	(10)	19.6	(6)	5.5	(6)	8.7	(15)	15.1	(2)	3.7	(82)	
Pneumococcus, untyped	(6)	5.0	(7)	8.3	(24)	10.3	(4)	7.8	(2)	1.8	(3)	4.3	(11)	11.1	(3)	5.6	(60)	
M. catarrhalis	(3)	2.5	(3)	3.5	(34)	14.5	(9)	17.6	(6)	5.5	(1)	1.4	(5)	5.0	(4)	7.5	(65)	
Meningococcus	(1)	0.8	(0)	0	(0)	0	(0)	0	(0)	0	(2)	2.9	(2)	2.0	(0)	0	(5)	
Diphtheroids	(3)	2.5	(0)	0	(6)	2.5	(4)	7.8	(2)	1.8	(0)	0	(0)	0	(0)	0	(15)	
Staphylococcus	(4)	3.3	(2)	3.3	(18)	7.5	(1)	1.9	(5)	4.5	(2)	2.9	(2)	2.0	(1)	1.8	(35)	
M. tetragenus	(0)	0	(1)	1.1	(2)	0.8	(1)	1.9	(0)	0	(0)	0	(1)	1.0	(0)	0	(5)	
Total number organisms found	(132)		(92)		(369)		(86)		(91)		(52)		(125)		(44)		(991)	

TABLE 11.—Distribution and Incidence of Bacteria Present According to Duration of Disease (in Per Cent.)

	Organs																															
	Heart's Blood				Pleurae Right 45 Left 46				Lungs Right 117 Left 117				Bronchial Exudate				Spleen				Subarachnoid and Brain Ventricles				Accessory Nasal Sinuses and Mastoid Cells				Other Structures			
	Duration of Disease in Days				Duration of Disease in Days				Duration of Disease in Days				Duration of Disease in Days				Duration of Disease in Days				Duration of Disease in Days				Duration of Disease in Days				Duration of Disease in Days			
	1 to 5	6 to 10	11 to 15	16 to 40	1 to 5	6 to 10	11 to 15	16 to 40	1 to 5	6 to 10	11 to 15	16 to 40	1 to 5	6 to 10	11 to 15	16 to 40	1 to 5	6 to 10	11 to 15	16 to 40	1 to 5	6 to 10	11 to 15	16 to 40	1 to 5	6 to 10	11 to 15	16 to 40	1 to 5	6 to 10	11 to 15	16 to 40
Number examined..	8	49	24	26	10	48	17	15	16	98	60	60	3	34	16	10	2	47	28	31	4	23	25	20	4	32	30	47	2	11	6	20
B. influenzae..	25.0	36.7	29.1	11.5	10.0	18.7	29.4	0	25.0	45.9	23.3	18.3	33.3	26.4	56.2	30.0	100.0	34.0	17.5	6.4	0	8.6	8.0	10.0	25.0	18.7	46.6	14.9	50.0	27.2	66.6	5.0
Hemolytic streptococcus..	0	28.5	3.7	34.6	0	31.2	29.4	26.6	0	32.6	26.6	30.0	0	11.7	18.7	0	0	19.1	17.5	9.6	0	13.0	4.0	15.0	0	15.6	16.6	6.3	0	9.0	16.6	30.0
Nonhem. streptococcus....	25.0	30.6	29.1	26.9	10.0	25.0	35.2	46.6	56.2	36.7	35.0	25.0	33.3	14.6	50.0	40.0	50.0	17.0	21.4	16.1	25.0	26.0	24.0	25.0	75.0	3.4	36.6	14.9	0	27.2	33.3	5.0
Pneumococcus, Type I....	0	0	1.2	0	0	2.0	5.8	0	12.5	1.0	8.3	0	0	2.9	0	0	0	2.1	7.1	0	0	0	8.0	0	0	0	3.3	0	0	0	0	0
Pneumococcus, Type II...	0	4.0	8.3	3.8	0	2.0	5.8	0	0	6.1	6.6	3.3	0	0	6.2	0	0	0	0	0	0	0	12.0	0	0	0	6.6	4.2	0	0	33.3	0
Pneumococcus, Type IIs..	12.5	4.0	4.1	0	10.0	8.3	5.8	0	12.5	3.0	5.0	0	33.3	2.9	12.5	0	0	2.1	3.5	3.2	25.0	0	12.0	0	25.0	9.3	6.6	0	0	0	33.3	0
Pneumococcus, Type III..	0	2.0	0	3.8	0	0	0	0	0	5.1	0	3.3	0	0	0	10.0	0	2.1	0	0	0	8.6	0	5.0	0	3.1	0	2.1	0	0	0	5.0
Pneumococcus, Type IV...	12.5	4.0	8.3	19.2	10.0	2.0	11.7	13.3	12.5	5.1	8.3	21.6	33.3	2.9	12.5	40.0	50.0	4.2	3.5	3.2	0	4.3	0	15.0	0	9.3	23.3	10.6	0	0	0	0
Pneumococcus, untyped...	12.5	6.1	0	7.6	30.0	6.2	11.7	0	18.7	18.3	5.0	5.0	0	11.7	18.7	30.0	0	6.3	0	0	0	4.3	4.0	0	0	9.3	9.9	4.2	50.0	9.0	16.6	0
Pneumococcus, total.....	37.5	20.1	21.9	34.4	50.0	20.5	40.8	13.3	56.2	38.6	33.2	33.2	66.6	20.4	49.9	80.0	50.0	16.8	14.1	6.4	25.0	17.2	36.0	20.0	25.0	31.0	49.7	21.1	50.0	9.0	83.2	5.0
M. catarrhalis..... ..	0	0	4.1	7.6	20.0	0	5.8	0	37.5	11.2	6.6	15.0	33.3	5.8	18.7	20.0	0	2.1	0	16.1	0	0	4.0	10.0	0	6.2	0	6.3	50.0	9.0	16.6	5.0
Meningococcus.....	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	8.0	0	0	0	0	0	0	0	0	0
M. tetragenus.....	0	0	0	0	10.0	0	0	0	0	2.0	0	0	0	0	6.2	0	0	0	0	0	0	0	0	5.0	0	0	0	0	0	0	16.6	0
Diphtheroids.....	0	0	4.1	3.8	0	0	0	0	0	1.0	5.0	3.3	0	2.9	12.5	10.0	0	4.2	0	3.2	0	0	0	5.0	0	0	0	0	0	9.0	0	0
Staphylococcus.....	0	0	4.1	3.8	0	0	0	0	12.5	8.1	3.3	11.6	0	0	0	10.0	50.0	2.1	0	3.2	0	4.3	0	0	0	3.1	0	4.2	0	0	0	5.0

Early in October, 1918, the sputum of 129 influenza patients was examined (Table 12). It will be seen that in the early days the hemolytic streptococcus was not very prominent, showing in 5 per cent., whereas the trinity of *B. influenzae*, nonhemolytic streptococcus and pneumococcus, and of those typed, Type IV constituted 76.9 per cent., were very much the most prominent organisms. One hundred and fifty other sputums sent to the laboratory routinely during October and November show *B. influenzae* 9.4 per cent., and hemolytic streptococcus in 33 per cent., indicating how much oftener hemolytic streptococcus was generally found than in the actual influenza cases.

TABLE 12.—Sputum Examination from Influenza Patients During October, 1918 *

Total examinations, 729 Organisms	Number	Per Cent.	
B. influenzae	315	43.2	
Hemolytic streptococcus	39	5.3	
Nonhemolytic streptococcus	309	42.3	
Pneumococcus, Type I	7	13.4	
Pneumococcus, Type II	2	3.8	of those
Pneumococcus, Type III	3	5.7	typed
Pneumococcus, Type IV	40	76.9	
Unsuitable for typing	447	61.3	
Pneumococcus, total	499	68.4	
Staphylococcus	191	26.2	
M. catarrhalis	99	13.5	
M. tetragenus	5	0.7	

* In the great majority of instances these sputums were unsuitable for type determination, being thin and unwashable. Also they were taken in such quantities and in so brief a time that with the force at our command we could only select the best specimens which showed as nearly as possible pure culture.

TABLE 13.—Incidence of Organisms in Throats of 250 Cases of Influenza (First Ten Days of Epidemic, from September 21 to October 1)

	Number	Per Cent.
B. influenzae	45	18.0
Hemolytic streptococcus	13	5.2
Nonhemolytic streptococcus	76	30.4
M. catarrhalis	82	32.8
Staphylococcus	43	17.2
Pneumococcus	44	17.6

In the very first ten days of the epidemic (from September 21 to October 1) swabbings from the throats of 250 influenza cases were taken (Table 13). It is remarkable how closely the findings simulate those of the sputum from the same class of patients taken during the ensuing ten days or so. Here again the hemolytic streptococcus was found in only 5 per cent., while nonhemolytic streptococcus, *M. catarrhalis* and *B. influenzae* together with pneumococcus and staphylococcus in lesser degree were the most prominent. In other words, the organ-

isms which we consider to be most responsible are most evident even in the initial swabbings before the epidemic had broken in its full fury upon us.

It is interesting to note from our records that in two months—January and February—following the epidemic, 178 sputum examinations were made with the following findings:

Pneumococcus	71.9 per cent.
Hemolytic streptococcus	33.4 per cent.
Nonhemolytic streptococcus	30.8 per cent.
Bacillus influenzae	6.7 per cent.
Staphylococcus	45.5 per cent.
Micrococcus catarrhalis	58.9 per cent.

One hundred and sixteen pneumococci were typed as follows:

Type I	1 case
Type II	4 cases
Type IIa	0 case
Type III	3 cases
Type IV	108 cases
Untyped	12 cases

Thirty-three necropsies for the same period showed:

	Heart's Blood, No. Cases	Lungs, No. Cases	Spleen, No. Cases	Pleural Cavities, No. Cases
Pneumococcus	2	3	0	1
Hemolytic streptococcus	17	22	12	9
Nonhemolytic streptococcus	5	5	0	0
B. influenzae	1	1	0	0
Staphylococcus	2	4	0	1
Micrococcus catarrhalis	1	3	1	1

These last are very interesting as showing the extraordinary predominance of hemolytic streptococcus to the exclusion of the main factors during the epidemic. As regards the overwhelming preponderance of Type IV pneumococcus in these more recent sputum examinations, it should be remembered first, the liability to salivary contamination, and second, in the present wave of enthusiasm for type determination of pneumococcus we are unconsciously subscribing to the premise that it alone, when present, is responsible for the pathologic condition, often overlooking entirely the more dangerous cohabitant. It is worthy of note, too, how the *B. influenzae* has almost disappeared from both necropsy and sputum findings. It should be remarked that these latter statistics contain a very few cases of undoubted influenza, so the presence of bacillus of Pfeiffer in small percentages is agreeably accounted for.

Lastly, we come to the consideration of five cases which lasted forty days or more. In every one of these cases hemolytic streptococcus was the offending organism. In four cases it was recovered

from the heart's blood. In one it was associated with *M. catarrhalis* in the left lung. But with this exception they were all five pure hemolytic streptococcus infections. This bears out our contention that hemolytic streptococcus was a tertiary invader, and by its luxuriant growth supplanted the original organisms.

SUMMARY AND DISCUSSION

While no attempt has been made to collect all the bacteriologic literature it seems desirable to review a number of the reports on the present pandemic for purposes of comparison. The previous great pandemic has been so ably presented by Kolle and Wassermann[62] that we may well omit it from our present discussion. Selter,[63] of Königsburg, experimenting on himself and a woman assistant, Nicolle and LeBailly,[64] and later Rivière,[65] Gibson and Connor[66] published results which would seem to suggest the possibility of a filtrable virus, but their findings are not altogether identical and are contradicted in their entirety by the experiments of Rosenau and Keegan[67] on nine volunteers from the Deer Island Naval Station, men who had not previously been exposed to the disease, and therefore were eminently suitable subjects. The experiments on a much larger body of men at San Francisco,[68] men who had previously been inoculated with a protective vaccine of *B. influenzae,* pneumococcus and streptococcus, were likewise entirely negative. Further contradiction is furnished by the negative results of Nuzum et al.[21] at the Cook County Hospital.

On the other hand, Keegan[67] recovered the *B. influenzae* in a series of twenty-three necropsies, from the lungs in 82.6 per cent. of the cases, in 31.6 per cent. of which it was in pure culture. In our series it was recovered pure from both lungs in two cases, and these were early in the epidemic. In both these cases it was recovered from the heart's blood and all other organs examined with positive results, viz., spleen and pericardium.

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62. Kolle and Wassermann Handbuch d. pathogenen Mikroorganism, Jena, Gustav Fischer, 1914.

63. Selter, H.: Zur Aetiologie der Influenza, Deutsch. med. Wchnschr. **43**: 932, 1917. Quoted by British Research Committee.

64. Nicolle, C., and LeBailly, C.: Quelques notions Expérimentales sur le virus de la Grippe, Compt. rend. Acad. d. sc., **167**:607, 1918.

65. Dugarric de la Rivière, R.: La Grippe, est elle une Maladie à virus filtrans? Compt. rend. Acad. de sc. **167**:606, 1918.

66. Gibson, and Connor, J. I.: Filtrable Virus as Cause of Early Stage of Present Epidemic of Influenza, Brit. M. J. **2**:645 (Dec. 14) 1918. Etiology of Influenza, Brit. M. J. **2**:331 (March 22) 1919.

67. Keegan: The Prevailing Pandemic of Influenza, J. A. M. A. **71**:1051 (Sept. 28) 1918.

68. U. S. Navy at San Francisco: Some Interesting, Though Unsuccessful, Attempts to Transmit Influenza Experimentally, Pub. Health Rep. **34**:33, 1919.

The Conference of Bacteriologists at the British War Office under Col. Sir William Leishman,[69] while not altogether satisfied as to the primary etiologic significance of *B. influenzae,* had no doubts as to its frequent presence in the epidemic and the great importance of the part it played in the production of symptoms and complications. Synnott and Clark[70] from Camp Dix report, "Bacillus of Pfeiffer has been encountered in the majority of cases *when looked for.*" "It has been recovered from the lung substance, the bronchi, the trachea and sputum, but from none of over 300 blood cultures." "In no case was it the sole invading organism . . ." "Whatever rôle *B. influenzae* plays in the present epidemic it does not invade the blood, and in all probability cannot solely be responsible for the fatal termination . . ." with most of which, with the modification that it can and does invade the blood and is capable alone of forming a fatal pneumonitis, we are in accord.

Hall, Stone et all.[29] reporting seventy-nine uncomplicated cases of influenza, found in the sputum the following: *B. influenzae* fifty-eight times, pneumococcus seventy-six times, *M. catarrhalis* thirty-nine times, hemolytic streptococcus four times and in nine necropsies they recovered from the lungs: Pneumococcus four times, *B. influenzae* once, hemolytic streptococcus once, and had negative results thrice. Their sputum and throat findings are similar to our own in that they show the relative infrequency of the hemolytic streptococcus. It is surprising that the nonhemolytic streptococcus was not reported at all, and we are inclined to wonder if it has been included under the head of pneumococcus, as has been done in other reports, notably that of Keegan[68] who places his reliance on morphology, thus, no doubt, including as Type IV pneumococcus many such organisms as in our report are set down as nonhemolytic streptococcus. Blanton and Irons,[10] in reporting the bacteriology of heart's blood and lungs in 280 pneumonitis cases at necropsy, recovered the hemolytic streptococcus more frequently than the nonhemolytic streptococcus, lungs 76.66 and heart's blood 64:48, respectively; *B. influenzae* was recovered eight times from the lungs and twice was the sole organism present. In the heart's blood it was found three times, once alone. Here we have three cases of pure influenzal pneumonitis, as against our two. Their streptococci sugar reactions are in no wise comparable with ours, as they did not find any mannite fermenters.

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69. London Letter: Quoted in J. A. M. A. **71**:1759 (Nov. 23) 1918.
70. Synnott, M. J., and Clark, E.: Influenza Epidemic at Camp Dix, J. A. M. A. **71**:1816 (Nov. 30) 1918.

The experiments of Julia Parker[71] would seem to indicate that the *B. influenzae* excretes a filtrable exotoxin, and if confirmed, constitute a very valuable addition to our knowledge. Stone and Swift,[13] at Fort Riley, implicate *B. influenzae* or an unknown virus as the etiologically responsible agent. The experiences of Base Hospital No. 17,[72] in France, indicated the primary importance of the Pfeiffer bacillus in this epidemic, as do editorials in the *British Medical Journal.*[73] Averill, Young and Griffiths,[74] in a report before the Medical Research Committee of Great Britain, gave 75 per cent. *B. influenzae* in forty-three cases; pneumococci also constituted 75 per cent. of the findings. Dietrich and Neisser[75] found *B. influenzae* in 100 per cent. of seven necropsies. The Budapest Clinic[76] claims to have isolated the bacillus of Pfeiffer from every case examined. Rapoport[77] found *B. influenzae* in over 80 per cent. of his necropsies and showed the presence of antibodies in 54.5 per cent. out of 295 convalescents, whereas, of 300 control serums only 9.6 per cent. fixed complement. These figures, if confirmed, are a strong argument in favor of those who still believe that the Pfeiffer bacillus is the prime causal agent. Stillman and Pritchett,[78] using Avery's[58] oleate medium, cultivated *B. influenzae* in 93 per cent. of cases of influenza and bronchopneumonitis. Incidentally, they also recovered it in 43 per cent. of normal individuals. In uncomplicated influenza it was recovered in 83 per cent. of forty-nine cases; in influenza with bronchopneumonia, in 93 per cent. of forty-three cases; in bronchopneumonia in 100 per cent. of six cases, and in lobar pneumonia in 55 per cent. of twenty cases. The Kitasato Institute[79] considers *B. influenzae* the cause of the pandemic. They found the bacillus of Pfeiffer in pure culture in the nasal cavities of patients. Hicks and Gray,[80] too, encountered the *B. influenzae* in high percentage in their series of cases—80 per cent. in the nasopharynx and 75 per cent. in the sputum.

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71. Parker, Julia: A Filtrable Poison Produced by Bacillus Influenza (Pfeiffer), J. A. M. A. **72**:476 (Feb. 15) 1919.

72. Weekly Bulletin, A. E. F., No. 27, 1918.

73. Brit. M. J. Editorials **2**: Paragraphs 39 and 91, 1918.

74. Averill, Young, Griffiths: The Influenza Epidemic in a Camp, Brit. M. J. **2**:111 (Aug. 3) 1918.

75. Dietrich, A.: Pathologische-anatomische Beobachtungen über Influenza im Felde, München. med. Wchnschr. **65**:928, 1918. Quoted by Brit. Med. Res. Committee.

76. Quotation from Report of Brit. Med. Res. Committee.

77. Rapoport, F. H.: The Complement Fixation Test in Influenzal Pneumonia, J. A. M. A. **72**:633 (March 1) 1919.

78. Stillman and Pritchett: J. Exper. M. **29**:259 (March) 1919.

79. Okawara, I., Tanaka, T., et al.: Kitasato Arch. Exper. Med., **2**:235, 1918.

80. Hicks, A. B., and Gray, L.: Influenza in Woolwich District, Lancet **2**:419, 1919

So far the evidence implicating the bacillus of Pfeiffer has been very strong. On the other hand, Bircher[81] indicates streptococcus. Uhlenhuth[82] only made cultural recovery of *B. influenzae* in 13 per cent. of his sputums, and once he found it in an empyema and a throat swab. His blood cultures were negative. Rosenow[83] found the green producing lanceolate diplostreptococcus, for which Tunnicliff[84] finds increased opsonic content in the serum of recovered cases. Stitt[85] failed to find antibodies for various strains of *B. influenzae*, and from Camp Fremont, Brem[86] et al., while frequently finding *B. influenzae*, consider an ultramicroscopic filtrable virus to be the responsible agent, with as secondary complicating organisms, the hemolytic streptococcus, the nonhemolytic streptococcus, Type IV pneumococcus, and, in bronchopneumonia, *B. influenzae*. Ely, Lloyd et al.[87] consider the hemolytic streptococcus to be the cause, for in twenty postmortems they found the hemolytic streptococcus in the heart's blood seventeen times. Their findings would agree with ours in the latest periods of the epidemic, and in the long protracted cases where *B. influenzae* had died out or been replaced. Pfeiffer[88] reports findings of his bacillus inconstant. MacCallum[44] considers that in some regions *B. influenzae* was a particularly common secondary invader, in others it was insignificant. But, apparently, he has not considered the time period at which the investigations were made. Simmonds[89] found it in both sputum and postmortem material "very frequently." He also reports secondary streptococcic infection to be more common than in the pandemic of 1890.

Taking a few consecutive cases at any one period of the epidemic as manifested here, we could reproduce the exact picture as reported from any one of the above quoted observers. In the early days we

81. Bircher, E.: Influenza Epidemic, Corr.-Bl. f. schweiz. Aerzte **48**:1338, 1918.

82. Uhlenhuth: Zur Bakteriologie der Influenza, Med. Klin. **14**:777, 1918. Quoted by Brit. Med. Res. Committee.

83. Rosenow, E. C.: Prophylactic Inoculation Against Respiratory Infections, J. A. M. A. **72**:31 (Jan. 4) 1919.

84. Tunnicliff, Ruth: Phagocytic Experiments in Influenza, J. A. M. A. **71**: 1733 (Nov. 23) 1918.

85. Stitt, E. R.: American Public Health Association. Quoted in J. A. M. A. **71**:2098 (Dec. 21) 1918.

86. Brem, W. V., Bolling, G. E., Caspar, E. J.: Pandemic Influenza and Secondary Pneumonia at Camp Fremont, Calif., J. A. M. A. **71**:2138 (Dec. 28) 1918.

87. Ely, C. F., Lloyd, B. J., Hitchcock, C. D., Nickson, O. H.: Influenza at Puget Sound Navy Yard, J. A. M. A. **72**:24 (Jan. 4) 1919.

88. Pfeiffer: Quoted by Brit. Med. Res. Committee.

89. Simmonds, M.: Zur Pathologie der diesjährigen Grippe, München. med. Wchnschr. **65**:873, 1918.

were discussing the predominance of the bacillus of Pfeiffer or the nonhemolytic streptococcus, the latter gathering strength as the former subsided (Table 9). Then as these in turn slowly dwindled, *Micrococcus catarrhalis* began to attain some prominence in the third period, followed in the fourth by an explosion of hemolytic streptococcus and staphylococcus. There is a rather curious flurry in the fourth period, i. e., the appearance of *B. influenzae* in the heart's blood of eight of thirty-three cases. We explain this by the fact that there were several fulminating cases at that time, which also coincided with the height of the epidemic in the neighboring town of Louisville, Ky. Of the fifty-seven cases of less than ten days' duration, while the majority fell in the earliest part of the epidemic, a large minority appeared in the fourth period, and in these the original invaders were not supplanted by the tertiary organisms, hemolytic streptococcus and staphylococcus, so common at that time.

Our sputum charts, submitted above, give added force to the necropsy picture. It must be remembered that our methods and media were the same at the beginning of the epidemic as they had been during the previous winter of 1917-1918, and yet, the Pfeiffer organism had only rarely been encountered. With the coming of the epidemic came also this organism, in large amount at first, and then as our cultural methods and media were improved to meet the situation, it began to decline in frequency of appearance unto almost the vanishing point. It is our belief that if we had the Avery[61] oleate medium in the last days of September, 1918, our findings in this respect would have easily been doubled.

CONCLUSION

1. The incidence of influenza is greater among whites than among negroes, but the mortality rate is higher among the latter.

2. The average duration of life is fourteen days; in the early part of the epidemic the average duration of life is considerably shorter, and in the latter part considerably longer.

3. The anatomic and bacteriologic findings vary with the stage of the epidemic and of the disease, and depend to a certain extent on the endemic bacterial flora. Earlier in the epidemic the disease was more fulminating, and during this time the *Bacillus influenzae* was most often found; as the epidemic progressed and the attacks lengthened, secondary invaders appeared more and more frequently and corresponding anatomical changes were found.

4. Influenza produces widespread changes throughout the body, and while the lungs commonly present the most spectacular lesions,

pronounced alterations are also encountered in the nervous, cardiovascular and other systems.

5. The most general changes produced by influenza are pronounced congestions, hemorrhages, toxic degenerative lesions and hemorrhagic inflammations. Hyperemia and hemorrhages are especially striking in the meninges, brain, serous membranes (petechial hemorrhages), skin (intense cyanosis, purpura hemorrhagica), lungs, spleen, liver and kidneys. Examples of toxic degenerations are Zenker's hyaline degeneration of the rectus muscles, conglutination and hyaline thrombosis, hyaline degeneration of vascular walls, hyaline degeneration of germinal centers of splenic follicles, focal necrosis of the liver, pancreas and suprarenal, toxic ganglionic changes and edema in the nervous system, and cloudy swelling of parenchymatous organs. Hemorrhagic inflammations are exemplified in early pneumonitis and pachymeningitis; productive inflammations are uncommon and confined to the later stages of the disease.

6. The true pneumonitis of influenza is characterized by extreme proliferation of pulmonary epithelium, pronounced hyperemia and hemorrhages. The commonly present secondary invaders produced a pneumonitis which grossly and microscopically consists of a number of separate, dissimilar pathologic processes. Macroscopically, a lobular pneumonia, with a tendency to become pseudolobar, and with a mixed, smooth and granular cut surface, is present. Microscopically, there are four distinct types of exudates, often within the same microscopic section, but distinctly independent. These are: catarrhal, fibrinocatarrhal, fibrinopurulent and purulent in type.

7. Throughout the disease there is a relative paucity of polymorphonuclear leukocytes and a proliferation of the lymphoid tissue; this would seem to point to myeloid intoxication and to lymphoid stimulation.

8. Chronic influenza is characterized by relative absence of vascular changes, connective tissue proliferation and diffuse suppuration.

9. The influenza bacillus, although not found in every case, was present in a sufficiently high percentage, and often enough in acute fatally ending infections to consider it, if not the prime cause, at least the most important indicator of epidemic influenza. At all events its appearance with the epidemic and its relative absence prior thereto, using the same cultural methods, strongly strengthens the assumption of its pathogenic rôle.

10. *Bacillus influenzae* was easily cultivated early in the epidemic and during the recrudescence of the last period, and this corresponded with the fulminating pathology of these stages.

11. As the patients lived longer and the epidemic progressed, bacterial agents, well established at this post as the cause of respiratory tract disease, notably the nonhemolytic streptococcus and pneumococcus, appeared as secondary invaders and modified the bacterial readings and anatomic changes.

12. The nonhemolytic streptococcus, it should be stated, was a frequent commensal in the earliest part of the outbreak.

13. It is noteworthy that all the above secondary invaders were more fatal in symbiosis than alone.

14. Later in the epidemic the hemolytic streptococcus assumed the ascendency, as a tertiary invader crowding out the secondary invaders, and was of especial importance in cases of long duration. Staphylococcus and *M. catarrhalis* made their appearance toward the end of the epidemic and to some extent modified the pathology.

We wish to enter a plea for the reading and recording of total bacterial flora and their symbiotic relationships; by this means too great weight would not be placed on single observations, like typing of pneumococci. Furthermore, in the study of this disease, observation should be made on the stage of the epidemic and the individual cases. By this method the proper relations of the various organisms can be calculated.

We wish to express our grateful appreciation for the constant advice and constructive criticisms of Major Herbert Fox, Chief of the Laboratory Service, at whose request the writers pursued this investigation. To Dr. Fred Weidman, of the University of Pennsylvania, our thanks are due for the considerable pains he took in photographing our material.

A STUDY OF THE INCIDENCE OF PULMONARY TUBERCULOSIS IN SOLDIERS WITH IRRITABLE HEART *

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There is a superficial resemblance between the symptoms of "irritable heart of soldiers" and those of active pulmonary tuberculosis. Ready fatigue, breathlessness, tendency to excessive sweating, tachycardia, and symptoms of asthenia are common to the two conditions. Pain in the left chest, however, which is one of the commonest symptoms of irritable heart, is not characteristic of pulmonary tuberculosis. In the careful study of the history of men with irritable heart, a background of neurotic symptoms, neurologic disease, mental inferiority, emotional instability or psychic maladjustments is almost invariably discovered. Such conditions are, of course, not characteristic of pulmonary tuberculosis.

In a recent report, Warfield and Smith[1] found evidences of pulmonary tuberculosis in a large number of men with the diagnosis of irritable heart or some other synonym of "soldiers' heart." In 235 cases of irritable heart, pulmonary tuberculosis was found in eighty-eight. In forty-one cases, exercise brought out positive chest findings and rise of temperature, and the authors felt that, had intensive study of the whole group been possible, the incidence of pulmonary tuberculosis would have been larger.

This report calls attention to the important fact that before the diagnosis of irritable heart can be made, a careful general examination must be done in order to determine whether the symptoms can be explained by any existing organic disease. The diagnosis of irritable heart must be made largely by excluding certain other conditions; the two conditions that are probably most important are hyperthyroidism and pulmonary tuberculosis. It should be possible, especially with the diagnostic accessories of a hospital, to sort out cases of active tuberculosis of the lungs with a fair degree of accuracy.

After this preliminary sorting out of organic disease, however, there remains the group of men with the symptom complex of irritable heart and no demonstrable organic disease. This group is represented

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* This work was done under the direction of Capt. Bertnard Smith in the general study of Irritable Heart at U. S. Army General Hospital No. 9, Lakewood, N. J.

1. J. A. M. A. **71**:1815 (Nov. 30), 1918.

in Warfield and Smith's report by 147 men in whom tuberculosis was not found; no evidence is brought to show that tuberculosis plays any rôle in producing the symptoms of which these men complain.

On hypothetical grounds one might explain some of the symptoms of irritable heart by inferring or assuming the presence of healed or latent pulmonary tuberculosis. Extensive fibroid changes in the lungs might produce breathlessness and fatigue; the other symptoms would be more difficult to explain on this basis. It seems unlikely that pulmonary lesions of extent sufficient to cause the symptoms of irritable heart would elude careful physical examination, but it is conceivable, and this report is made with the purpose of contributing some observations on this subject.

At General Hospital No. 9, 246 cases of irritable heart have been studied. A careful history and physical examination was made in each case, directed, not only toward the cardiac condition, but toward the general condition of the patient as well. Each of these men was under observation for a period of weeks. During this time, they were given graded physical exercises, and temperature readings were made regularly. As the result of such observations, no man was found to have active pulmonary tuberculosis on admission. Two men with active lesions were admitted to the cardiac service of this hospital, but both happened to have organic heart disease.

Effect of Influenza.—Among the group of soldiers believed to have irritable heart, two developed active pulmonary tuberculosis following influenza. Both these men had been under observation for tuberculosis, as one of them had tuberculous glands of the neck and the other had had a recent pleurisy. Neither of these men showed symptoms, physical signs, or fever suggesting pulmonary tuberculosis until after influenza, when they developed typical symptoms and signs. The assumption in connection with these two cases is that the influenza caused activation of a tuberculous focus that had escaped detection before the acute infection. It is not, however, safe to infer that pulmonary tuberculosis was the cause of these men's complaints before the influenza. Influenza is a severe pulmonary infection, and one that is likely to attack the integrity of the lungs in a very searching manner, and the tuberculosis that follows it might arise in a small and previously healed focus. Influenza attacked thirty-seven other men with irritable heart, all of whom made an uneventful recovery.

It has been said that pulmonary tuberculosis in the active stage was found in no patient sent into the cardiac wards of this hospital with irritable heart. Healed tuberculosis of the lungs was found in one case. In this case, the diagnosis was made by both physical examination and

FINDINGS OF HISTORY, PHYSICAL AND ROENTGEN-RAY EXAMINATION

Name	Family and Past History	Physical Examination	Roentgenogram of Lungs
C. E.	One sister died of pleurisy	Negative for tuberculosis	Few calcifications at hilums, otherwise negative
C. C.	Negative	Negative for tuberculosis	Some calcified glands at hilums; slight infiltration; negative for tuberculosis
F. J.	Negative	Negative for tuberculosis	Negative
F. J.	Negative	Negative for tuberculosis	Hilus thickening; apices clear
G. G.	Grandfather, maternal grandmother and 1 aunt died of tuberculosis	Negative for tuberculosis	Few calcified glands at right hilus; otherwise negative
H. E.	Negative	Negative for tuberculosis	Negative
L. W.	One brother had tuberculosis (doubtful); never ill, except acute bronchitis 1 yr. prior; now has chronic cough, mucus expectoration, at times bloodstreaked	No abnormal findings	Calcified glands at hilums; considerable peribronchial thickening, extending to periphery in right lower lobe, up to clavicle on right; probably not tuberculosis
L. W.	Negative	Negative	Normal peribronchial thickening; no tuberculosis
L. S.	Negative	Negative for tuberculosis	Negative
M. J.	Negative	Negative for tuberculosis	Peribronchial shadows right lower lobe; negative for tuberculosis
M. R.	Negative	Negative for tuberculosis	Calcified glands right hilus; pleural thickening right base; negative for tuberculosis
M. A.	Negative	Negative for tuberculosis	Negative for tuberculosis
M. H.	Negative	Negative for tuberculosis	Peribronchial shadows right lower lobe; negative for tuberculosis
M. W.	Negative	Negative for tuberculosis	Some peribronchial thickening; negative for tuberculosis
M.	Negative	Negative for tuberculosis	Peribronchial thickening right lower lobe; not reaching to diaphragm; negative for tuberculosis
T. P.	Negative	Negative for tuberculosis	Bronchial shadows right lower lobe, not tuberculous
T. W.	Negative	Negative for tuberculosis	Slight thickening of both hilums; negative for tuberculosis
H. H.	Negative	Negative for tuberculosis	Some peribronchial thickening, especially in bases, following influenza; negative for tuberculosis
W. E.	Negative	Negative for tuberculosis	Slight hilus thickening; no tuberculosis
G. M.	Negative	Negative for tuberculosis	Hilus thickening; negative for tuberculosis
S. S.	Father died tuberculosis; 1 brother has tuberculosis; past history negative.	Negative for tuberculosis	Slight bronchial thickening, extending to clavicle on right; negative for tuberculosis
C.	Negative	Negative for tuberculosis	Considerable peribronchial thickening, extending to periphery. No spotty infiltration; negative for tuberculosis
H.	Negative	Negative for tuberculosis	Not done
M.	Not obtained	Negative for tuberculosis	Hilums thickened; negative for tuberculosis
W.	Negative	Negative for tuberculosis	Slight infiltration, especially of right base; negative for tuberculosis
W.	Negative for tuberculosis	Signs of tuberculosis, pulmonary, chronic, inactive, right upper lobe	Marked thickening about roots of both lungs, and extension from hilus to middle of left lung. Apices clear; spotty infiltration up to clavicle on right; probably old tuberculosis
Mc.	Negative	Negative	Flat plate: slight thickening of hilums; negative for tuberculosis; stereoscopic plates: slight spotty infiltration of both apices, possibly tuberculosis
Z.	Family history negative; doubtful hemoptysis 6 mos. prior; dry cough for past 4 mos., following gassing	Negative	Some bronchial infiltration of both lungs, not tuberculous
R.	Negative for tuberculosis	Negative	Some bronchial thickening, extending up to clavicles, probably not tuberculous
C.	Incomplete	Negative	Negative
LeC.	Negative	Negative	Negative
M.	Father died of pulmonary tuberculosis; history otherwise negative for tuberculosis	Negative	Negative

roentgenogram. This case happens to be included in the group described in the table, of men who were studied more carefully than was customary.

An unselected group of men with irritable heart was studied especially for indication of pulmonary tuberculosis. The results are shown in the table. The history consisted in inquiry for tuberculosis in the family, and for hemoptysis, chronic cough, loss of weight, pleurisy and so forth in past life. The physical examination consisted of careful examination of the lungs, including auscultation after cough.

Major J. Woods Price of Saranac made fourteen of the physical examinations tabulated above while on a visit to this hospital, and he has kindly consented to allow his findings to be incorporated. Stereoscopic roentgenograms were made in twenty-nine cases, flat plates in three. Lieuts. M. H. Glover and W. A. Newell have generously given their time for careful examination of these plates for tuberculosis. Five plates were also examined by Major Price.

Only one man showed evidence of pulmonary tuberculosis by physical examination; this consisted of a healed lesion at the right upper lobe. The roentgenogram in this case also showed tuberculous changes. Even counting this case, it is doubtful whether a group of healthy individuals would show any less evidence of tuberculosis than did these men with "irritable heart."

Summary.—1. In a group of 246 men with "irritable heart of soldiers" studied at this hospital, one was found with definite signs of arrested pulmonary tuberculosis. Two men of this group developed active pulmonary tuberculosis after influenza. No other diagnosis of pulmonary tuberculosis was made.

2. Intensive study of thirty-two cases of irritable heart showed arrested pulmonary tuberculosis in only one case, with no instance of active tuberculosis.

CONCLUSION

No evidence has been found, from the study of irritable heart at this hospital, that there exists more than an accidental relationship between this condition and pulmonary tuberculosis.

THE INCREASE OF EXTRACT NITROGEN IN THE TISSUES, WITH CHRONIC NEPHRITIS*

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It has been well established that one of the characteristic features of one type of chronic nephritis is the retention of nitrogen. This has been demonstrated in a number of different ways, beginning with the observation of Bright that there was an increase of urea in the blood. Modern methods have elaborated on the original findings and in recent years metabolic studies of these cases have shown a positive balance between intake and output of nitrogen. I have reported studies of this kind, demonstrating that with certain cases the retention may be more than one gram of nitrogen a day, when the protein intake is equivalent to 10 gm. of nitrogen per day.

It occasionally happens, with cases of this kind, that there is no commensurate increase in the nonprotein nitrogen of the blood during a period of observation. This gives rise to the question: where is this retained nitrogen stored? The mere fact of nitrogen retention with normal individuals can be explained in only two ways—growth; and the building of new tissues, as, for example, during periods of convalescence from some diseases. With individuals who are obviously sick, either of these explanations is untenable and some third possibility must be entertained. Again, it was observed, when these cases of chronic nephritis were studied according to metabolic methods, that during periods of nitrogen loss when the output considerably exceeded the intake, there was not always a drop in the nonprotein nitrogen of the blood nearly sufficient to explain the minus balance. We have many records showing a nitrogen loss of 0.3 gm. daily, over a period of two weeks—a total loss of more than 5 gm., and during this period the nonprotein nitrogen might not change within the limits of error or might drop 0.020 gm. per 100 c.c. For a person weighing 75 kilos, this would be a total loss of about 1.5 gm., perhaps, hardly more. For these reasons it seemed necessary to make a more exhaustive examination of the tissues in order to determine what became of this retained nitrogen.

It will be understood readily that a large number of the cases were studied before we were able to secure data on tissue analyses, since some of the patients studied did not die in the hospital, and many who did die, could not be examined postmortem. However, at the

* From the Medical Clinic of the New York Hospital.

present time we have tissue analyses from fourteen cases of nephritis which evidenced nitrogen retention during life and the tissues were examined chemically after death.

The chemical examination of these tissues was conducted not without considerable technical difficulty. It was impossible, of course, to examine samples of all the tissues of the body. On account of mass, it seemed reasonable to suppose that the muscles were implicated largely in nitrogen retention, and for theoretical considerations, liver analyses are desirable. The disturbances of the central nervous system in late nephritis, indicates the desirability of analyses of the brain.

Autolysis probably begins antemortem; at least we know that in certain organs it progresses with astonishing rapidity, postmortem. For this reason tissues were analyzed only when the necropsy was done within six hours after death. Even with this precaution, we found that results of the brain analyses for nonprotein nitrogen were so fluctuating, and that the water content was so extremely variable, that no dependable fact could be deduced. Accordingly, all of these results are thrown out. We are also somewhat doubtful about our analyses of liver tissues, because of extreme variability in water content. The tissues have to be minced prior to extraction, and in the process of mincing, blood and water are expressed, and this is a confusing element in manipulation. It is hoped that in the future this investigation of liver tissue can be carried out by a definite technic which I will here suggest for the benefit of anyone who may be interested in this subject.

It is possible, by using methods familiar to bacteriologists, to desiccate tissues after freezing. This method is used for pulverizing bacteria, and it could be applied to the analysis of liver tissue without great difficulty, if the necessary equipment were available. The liver tissue so desiccated could be pulverized and extracted.

Muscle tissue from the psoas muscle was employed, because of its relative freedom from fat. No particular difficulties were encountered in making these analyses, and the results seem clear cut.

Considerable difficulty was experienced in establishing a normal for these tissue analyses. Obviously, all cases showing any nephritis at necropsy had to be excluded—a majority, even when there had been no reason during life to suspect impairment of renal function. The result of our analyses appears to indicate that the normal for extract nitrogen is always less than 1.00 gm. per 100 gm. of dry substance. Tissue from cases of pneumonia often exceeded this figure to a slight extent, but the kidneys from these cases usually show cloudy swelling, and the question is, are they functionally normal. These analyses are not included in the table, since the interpretation is dubious.

There is a notable variation in the water content of muscle and all tissues, and the variation is most marked when edema is a possibility. On this account a basis of comparison is secured by computing the extract nitrogen per grams of dry substance (last column of table), the only basis of comparison where several variables are involved.

Analysis of Psoas Muscle

	Anatomic Diagnosis	Water, per Cent.	Total N_2 per Cent., Gm.	Extract N_2 per Cent., Gm.	Extract N_2 per Cent. of Dry Substance, Gm.
4.	Sepsis	72.9	2.92	0.24	0.88
5.	Peritonitis, acute	74.9	3.18	0.18	0.71
11.	Fractured skull; cerebral hemorrhage	74.8	3.16	0.22	0.87
9.	Bronchopneumonia; postoperative appendicitis	69.03	3.39	0.28	0.90
7.	Cerebral embolism; cardiac	72.6	3.46	0.31	1.13
15.	Acute nephritis (postscarlatinal)	78.11	3.34	0.38	1.73
20.	Parenchymatous nephritis	74.5	3.58	0.24	0.94
21.	Parenchymatous nephritis	84.5	2.83	0.22	1.69
24.	Parenchymatous nephritis, large white kidney	79.8	3.11	0.22	1.88
13.	Chronic nephritis, granular kidney	78.39	3.23	0.34	1.57
14.	Chronic nephritis, granular kidney	73.85	2.02	0.28	1.08
16.	Chronic nephritis, contracted kidney	78.86	3.04	0.38	1.79
17.	Hydronephrosis, chronic nephritis	78.23	3.30	0.36	1.65
3.	Cerebral hemorrhage, chronic nephritis	77.7	3.03	0.37	1.65
27.	No kidney	78.4	....	0.38	1.75

The first four analyses are cases selected from the control series. For this series, we used only such cases as gave no evidence of renal disease during life and where, at necropsy, the kidneys were found to be relatively normal.

In Case 7 there was a slight increase of the nonprotein nitrogen during life. No metabolic study could be carried out. It is interesting that the nitrogen retention found with decompensated cardiac disease (to which I have called attention in an earlier paper) should be manifested also by an increase of extract nitrogen in the tissues.

Case 15 is the only example of nephritis following directly on scarlet fever that I have been able to study with proper care. Clinically, this case was of a mixed type, since there were disturbances of both salt and nitrogen metabolism. The slightly elevated water content of the muscle indicates a residual edema. The high figure for extract nitrogen corresponds with the clinical and laboratory findings during life.

Cases 20, 21 and 24 were diagnosed during life as parenchymatous nephritis. The functional disturbances concerned the water and salt excretion, and there was the usual normal or low blood concentration of extract nitrogen. A fact of considerable interest was noted in the metabolism studies of these cases. All showed a slight plus balance. In this respect they are quite like mild cases of interstitial nephritis.

In no case of what seemed to be parenchymatous nephritis that we have been able to study, has there been the minus balance or equilibrium expected. All showed some retention. This retention was always slight, but if the period of observation were ten days or more, it became evident—provided the nitrogen intake was 15 gm. This was a matter of considerable speculation, and was one of the reasons for this tissue study. Cases 21 and 24 seem to confirm the metabolic studies; case 20 does not.

This patient (Case 20) was studied about two weeks before death. At the time of the metabolism studies there was general anasarca—later a diuresis occurred and the edema vanished (with water content of muscle), following this the patient had a convulsive seizure which ended in death.

It has been accepted that there is no significant disturbance of the protein metabolism to be noted in cases of pure parenchymatous nephritis. The evidence on which this conception rests is open to some question. The water content of blood is variable; when there is edema observations of specific gravity, water content and dry substance all indicate an hydremic condition of the blood. The customary technic for estimating the nonprotein nitrogen of the blood takes no account of this. A volume of blood, from 25 to 50 c.c., is measured and the extract nitrogen determined in this volume. Comparison of an hydremic blood with normal blood thus introduces an obvious error which we have long recognized and discounted in blood counts and hemoglobin estimations. For correct facts as to the nonprotein nitrogen of blood, the specific gravity of the blood, or the water content must be known, and from these computations derived as to nitrogen.[1]

The cases of chronic interstitial nephritis show, with one exception, an increase of extract nitrogen of 50 per cent. or more above normal. All of these patients had been treated by means of low nitrogen diets, and all had shown a negative balance for variable periods. The tissue accumulation is the more significant on this account.

The last case (Case 27) is of interest. The sole functioning kidney was removed on account of uncontrollable hemorrhage following an operation for perinephritic abscess. At necropsy the remaining kidney was found to be a fetal remnant about one inch in length and without functioning elements.

1. Some interesting computations may be made from data given in the paper of Butterfield (Am. J. M. Sc. **151**:63 (Jan.) 1916) dealing with the physical characteristics of blood from nephritic cases. With normals there is a specific gravity of 1.027, a dry residue of 9.8 per cent. and a protein content of 8.1 per cent.; when edema occurs with nephritis, then the specific gravity may fall to 1.015, the dry residue to 6.3 per cent. and the protein content to 4.3 per cent., nearly half the normal.

The data offered in this communication are neither complete nor conclusive. The evidence at hand simply supports an inference that has always been made, namely, that retained nitrogen cannot be retained exclusively in the blood. There seems also a possibility that disturbances of protein metabolism is a characteristic of nephritis generally, and that differences with types of nephritis are differences only of degree.

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